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ANTIBIOTIC PRESCRIBING
FOCUSING ON THE SITUATION IN SWEDISH NURSING HOMES

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ABSTRACT

Background The increasing rate of resistance to antibiotics has become a global concern. High consumption and irrational use of antibiotics is contributing to this development. In Sweden sales data of antibiotics was available, but there was a lack of detailed knowledge about therapeutic indications and compliance with guidelines, especially concerning elderly residents in nursing homes.

Aim The aim was to present the treatment of infections in outpatients and in the elderly in nursing homes, and further to develop and evaluate the effect of an educational intervention, aiming at improving treatment with antibiotics in Swedish nursing homes. The specific objectives were to: i) Present the treatment patterns regarding infectious diseases in outpatients (I) and elderly residents in nursing homes (II). ii) Through focus group discussions and collection of knowledge and attitude data, elucidate the decision making process for antibiotic prescribing in nursing homes (III), target the intervention and explore barriers and facilitators for behavioural change. iii) Evaluate the effect of the intervention on quantity and quality of prescribing in relation to available guidelines (IV)

Methods Paper I and II are cross-sectional studies describing the prescribing pattern in outpatients in five counties and in 58 nursing homes in Sweden, respectively. In paper III mixed methods are used – focus group discussions with ten nursing assistants, ten nurses and six general practitioners, and a knowledge- and attitude questionnaire. The study design used in paper IV is a cluster randomised controlled trial evaluating an educational intervention targeting physicians and nurses concerning antibiotic prescribing in nursing homes in Sweden.

Results In the outpatient setting, 59% of patients with infectious complaints were treated with antibiotics (Paper I). In nursing homes the corresponding figure was 84% (Paper II). Women with lower UTI were treated with a quinolone in 21% of the cases in the outpatient setting (Paper I) and 29% in nursing homes (Paper II). In 38% of the cases in nursing homes, an antibiotic was prescribed during an indirect contact with the physician. Half of the women with lower UTI in nursing homes, received a treatment which was not in line with the recommendations (Paper II). The focus group discussions (Paper III) have provided us with a perspective on the staffs' own experiences with regard to infections in nursing homes. The educational intervention had a modest effect on most outcome variables, including the primary outcome - proportion of quinolones for lower UTI in women - but reduced the proportion of infections treated with an antibiotic by 12% (Paper IV).

Conclusions In outpatients, the prescribing pattern in general seemed to be in accordance with the recommendations, although there is still some room for improvement. The educational intervention had a modest effect on most outcomes, including the primary outcome, but reduced the proportion of prescribed courses of antibiotics.

Keywords: antibiotic prescribing, outpatients, nursing homes, educational intervention, Sweden

SAMMANFATTNING – ABSTRACT IN SWEDISH

Antibiotikaförskrivning

med fokus på särskilda boenden för äldre i Sverige

Bakgrund Antibiotikaresistens är numer ett globalt folkhälsoproblem. En hög förskrivning och irrationell antibiotikaanvändning är kända bidragande orsaker till den ökade antibiotikaresistensen. När denna studie började fanns förskrivningsdata, baserat på uthämtade recept av antibiotika på apotek, men uppgifter om indikation kopplat till förskrivningen var bristfälliga inom öppenvården och i synnerhet var kännedomen om antibiotikaförskrivningen vid särskilda boenden för äldre liten.

Syfte Att presentera förskrivningsmönstret av antibiotika kopplat till diagnos inom öppenvård samt på särskilda boenden för äldre (säbo), samt att utveckla och utvärdera en intervention riktad till sjuksköterskor och läkare med syfte att förbättra antibiotikaförskrivningen inom säbo i Sverige.

Metod Den första studien var en deskriptiv studie som omfattade fem län där diagnos- och förskrivningsdata samlades in under en vecka i november 2000 för alla patienter som sökte med infektionssymtom inom öppenvården. Den andra studien var en deskriptiv studie där diagnos- och förskrivningsdata samlades in under tre månader 2003 på 58 säbo. Den tredje studien genomfördes under 2003 och 2004 och bestod av två olika delar: fokusgruppdiskussioner med 10 undersköterskor, 10 sjuksköterskor och sex läkare med anknytning till säbo samt en kunskaps-attitydenkät kring urinvägsinfektioner. Den fjärde studien var en klusterrandomiserad studie indelad i en kontrollgrupp och en interventionsgrupp, varav den senare fick ta del av en utbildningsintervention för de vanligaste infektionerna på säbo för att se om förskrivningsmönstret kunde förändras i linje med då gällande behandlings-rekommendationer. Datainsamlingen före interventionen genomfördes under 2003 och datainsamlingen efter interventionen 2005.

Resultat Inom öppenvården fick 59% av patienterna som sökte för infektionssymtom antibiotika. På särskilda boenden för äldre fick 84% av de som registrerades i studien antibiotika. Kvinnor med nedre UVI fick en kinolon, som i normalfallet ej är rekommenderad för den indikationen, i 21% av fallen inom öppenvården, medan 29% av kvinnorna på särskilda boenden fick en kinolon på indikationen nedre UVI. På säbo var läkaren inte på plats vid 38% av förskrivningstillfällena. Hälften av kvinnorna med nedre UVI på säbo behandlades inte enligt rekommendationerna. Fokusgrupp-diskussionerna gav oss personalens perspektiv på infektioner på säbo samt bidrog till utvecklingen av interventionen. Utbildningsinterventionen hade en blygsam effekt på de förutbestämda utfallsvariablerna, inklusive på primärutfallet - andelen kinoloner förskrivna på indikationen nedre UVI hos kvinnor - men andelen infektioner som antibiotikabehandlades minskade med 12%.

Slutsats Inom öppenvården pekade förskrivningsmönstret på en relativt god följsamhet till gällande rekommendationer även om vissa möjligheter till förbättring kunde ses. Utbildningsinterventionen hade en relativt blygsam effekt, men den totala andelen infektioner som antibiotikabehandlades minskade.

LIST OF PUBLICATIONS

I. Stålsby Lundborg C, Olsson* E, Mölstad S; Swedish Study Group on Antibiotic Use. Antibiotic prescribing in outpatients: a 1-week diagnosis-prescribing study in 5 counties in Sweden. Scand J Infect Dis. 2002; 34:442-8.

II. Pettersson E, Vernby Å, Mölstad S, Stålsby Lundborg C. Infections and antibiotic prescribing in Swedish nursing homes: A cross-sectional study. Scand J of Infect Dis. 2008; 40: 393-398.

III. Pettersson E, Lannering C, Freudenthal S, Stålsby Lundborg C. Urinary tract infections and antibiotic treatment in Swedish nursing homes. A study on nursing assistants', nurses' and general practitioners' perceptions. *Manuscript*

IV. Pettersson E, Vernby Å, Mölstad S, Stålsby Lundborg C. Can a multifaceted educational intervention targeting both nurses and physicians change the prescribing of antibiotics to nursing home residents? A cluster randomised controlled trial. *Submitted*

*Former family name of Eva Pettersson

CONTENTS

LIST OF ABBREVIATIONS

ASB	Asymptomatic bacteriuria
ATC	Anatomical therapeutic chemical classification system
CAP	Community acquired pneumonia
CDAD	Clostridium difficile associated disease
cfu/mL	Colony-forming units per milliliter
DDD	Defined daily dose i.e the assumed average maintenance dose per day for a drug used for its main indication in adults
DDD/TIND	Defined Daily Doses per 1000 inhabitants and day
Deff	Design effect
DPS	Diagnosis-prescribing study
EARS-Net	European antimicrobial resistance surveillance network
ESBL	Extended spectrum beta-lactamase-producing *Enterobacteriaceae*
GAS	Group A streptococci
GP	General practitioner
ICC	Intracluster correlation coefficient
IUC	Indwelling urinary catheter
KA	Knowledge- and attitude questionnaire
MRSA	Methicillin-resistant *Staphylococcus aureus*
NHAP	Nursing home acquired pneumonia
NHQ	Nursing home questionnaire
PcV	Phenoxymethylpenicillin, commonly known as penicillin V
PRP	Penicillin-resistant pneumococci
RTI	Respiratory tract infection
S, I or R	Categorisation of infectious agents as susceptible, intermediate or resistant to particular antibiotics
SANT	Swedish antibiotic nursing home trial
Sida	Swedish international development cooperation agency
SSTI	Skin- and soft tissue infection
Strama	Swedish strategic programme against antibiotic resistance
UTI	Urinary tract infection
VRE	Vancomycine-resistant enterococci

PREFACE

During the early 90s I started to take extra work as a nursing assistant at different nursing homes. First I worked in my home municipality of Piteå and later on during my MSc in Pharmacy studies at Uppsala University, in the Uppsala municipality. I really enjoyed my extra work and found it very meaningful – you always felt appreciated by the elderly – which was a nice feeling. I remember one Christmas my mother said to me: "Do you really have to work this Christmas too?" I really wanted to work and so I did. At the different workplaces I have had different experiences, which seemed to be related to characteristics of the staff working there, rather than organisational or economic factors. During my MSc in Pharmacy studies I took a great interest in microbiology and infections: eventually more specifically in the use of antibiotics, although then at a global level. I went to Lao PDR to do a minor field study for Sida, Swedish international development cooperation agency, and there I studied drug sales at the pharmacies and found a very high and irrational dispensing of antibiotics.

On my return to Sweden I found that there had been many studies on antibiotic use, infections and hygiene related to children and day care centres. Due to my background working in elderly care I felt I wanted to know more about the use of antibiotics among the elderly population. After my MSc in pharmacy studies I was admitted to Health Care Sciences postgraduate school at the Karolinska Institutet. Here I started to project the realisation of my studies on antibiotic use in Sweden and I was also working with data on antibiotic prescribing to outpatients, which was used in Paper I of this thesis. The research projects they could offer at the postgraduate school were however not in the research area on which I wished to focus. So I wrote an application and received a grant from Apoteket AB's Fund for Research and Studies in Health Economics and Social Pharmacy (grant number 177/02). When I started my doctoral studies I had a somewhat naive belief that I would find out the truth about antibiotic prescribing in nursing homes. The abbreviation of the name of the randomized controlled trial being a part of this thesis – Swedish Antibiotic Nursing home Trial – SANT – actually means "true" in Swedish. Learning more and more about the infectious panorama in outpatients and later on in nursing homes I chose to focus on the most common infections in nursing homes. In writing the project plan I believed that there was a consensus on how they should be treated. However the simple fact that the guidelines for treatment of urinary tract infections had not been updated since 1990, should have given me pause. Fortunately we had the time and the funding to do a pilot study before the main project started. During the pilot study my pharmacy world was turned upside down. The guidelines were not followed! And determining a diagnosis like lower urinary tract infection was not as straightforward as I thought - not in this patient group. I thought I had a project with infections that were easily diagnosed and simple to treat according to evidence based guidelines, and that any deviations there might be could be cured with a little input on the guidelines to the prescribers. I was wrong, but during the years I have worked within this thesis project, there has been some progress in evidence based medicine within the area of antibiotic prescribing.

Tage Danielsson*, once said: Without doubt you are not sane. And yes, I have had doubts that I would ever finalise the work that I started, as life interrupted. During these

*A famous Swedish actor, author, comedian and film director

years at the division of Global Health (IHCAR) I have had two wonderful children: Emma and Alice and I became the head of the five hospital pharmacies in Norrbotten county during the turbulent years of privatisation of Swedish pharmacies. This explains some of the years that I have worked with this thesis. My main paper about the intervention has taken a journey starting with British Medical Journal, BMJ, where it passed all the way to the hanging committee.

Although I could not find *A* truth, I found many truths and also new questions that I have put together in this thesis about antibiotic prescribing, with a focus on nursing homes in Sweden.

1 BACKGROUND

1.1 ANTIBIOTIC RESISTANCE

The increasing rate of antimicrobial resistance has become an issue of global concern [1-3]. It is well recognised that consumption and irrational use of antibiotics is one major contributing factor to this development [1, 4-9]. Measures have been taken, both nationally and internationally, to contain this trend [1, 10, 11]. The Swedish strategic programme against antibiotic resistance (Strama) was founded in 1995 to work towards rational antibiotic use [11, 12].

An increased resistance in some of our most common pathogens causing for example pneumonia, *Streptococcus pneumoniae*, urinary tract infections, UTI, *Escherichia coli*, and skin- and soft tissue infections, SSTI, *Staphylococcus aureus*, would mean an alteration in our treatment choices and eventually a lack of available antibiotics with which to treat. There are few new antibiotics being developed [13]. Consequences of antibiotic resistance are adverse events for the consumers, increased mortality and also excessive costs for the care providers [14, 15].

In Sweden the resistance rates are lower compared to many other countries [12]. But it has been shown that resistance is difficult to reverse, which means that it is necessary that measures be taken before the resistance rates begin to grow to levels that are difficult to manage [16]. Resistance in bacteria with compulsory notification under the Communicable Disease Act in Sweden are penicillin-resistant pneumococcal infection (PRP), *Enterobacteriaceae* producing extended spectrum beta-lactamases (ESBL), Vancomycine-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* infection (MRSA). In Sweden the rates of PRP seem to have stabilised. 402 cases of VRE were reported during 2009, which was a decrease from 2008, but still much more common than during the period 2000-2006 when 18-35 cases per year were reported. The number of reported ESBL and MRSA in 2009 has increased [Smittskyddsinstitutet - Swedish Institute for Communicable Disease Control]. The question is how much longer Sweden can contain the antibiotic resistance.

European Antimicrobial Resistance Surveillance Network, EARS-Net, is a network of national surveillance systems in Europe. It is coordinated and funded by European Centre for Disease Prevention and Control. Their interactive database allows presentation of selected data in tables, figures and maps [17]. The figures 1, 2 and 3 below are illustrative, both in the perspective of differences between the countries in the susceptibility pattern of some common pathogens to common antibiotics, and in the perspective that antibiotic resistance is not an isolated phenomenon, but a global concern that requires the collaboration of all countries to be able to curb the trend of increased antibiotic resistance.

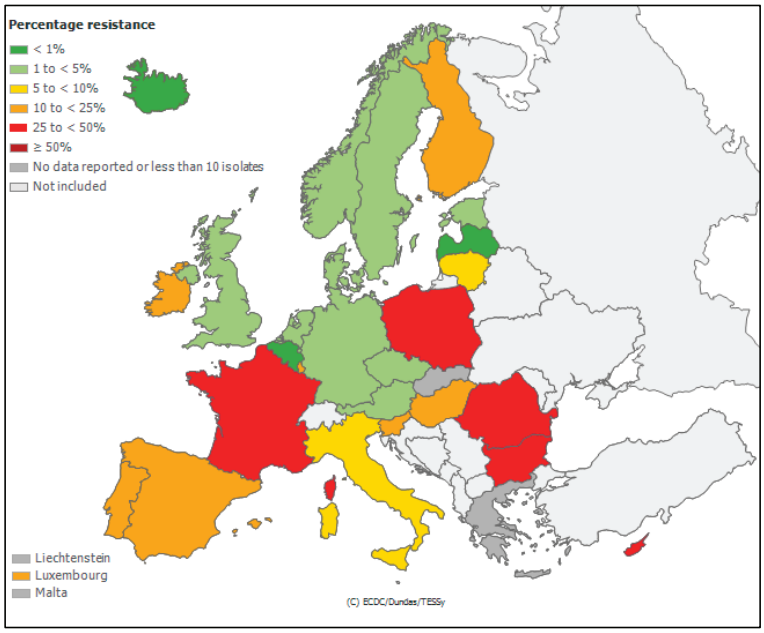


Figure 1. Proportion of Penicillins (R+I) resistant *Streptococcus pneumoniae* isolates in participating countries in 2009. *Source*: EARS-Net

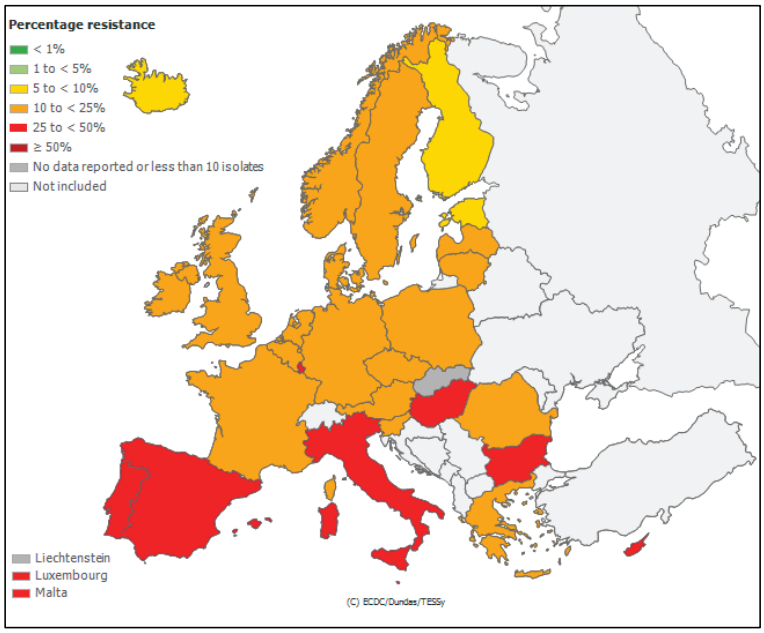


Figure 2. Proportion of Fluoroquinolones (R+I) resistant *Escherichia coli* isolates in participating countries in 2009. *Source*: EARS-Net

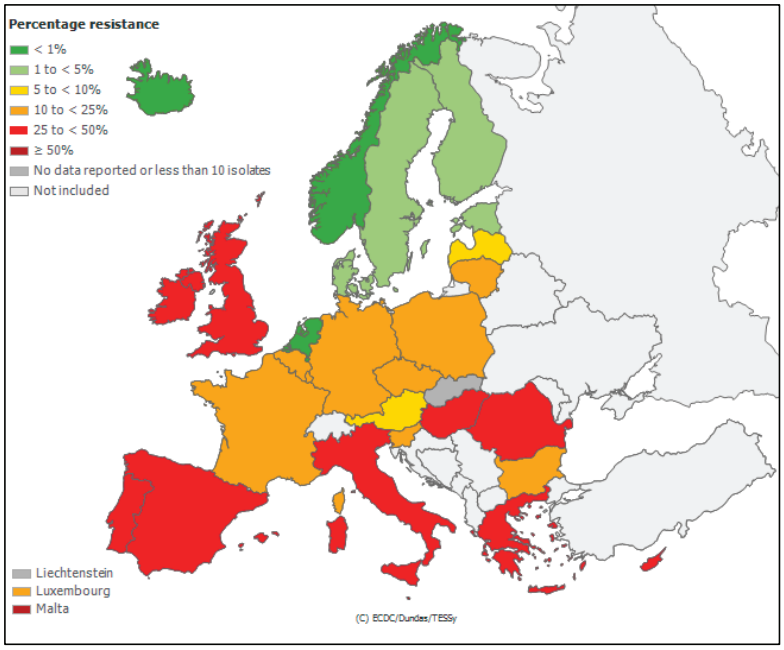


Figure 3. Proportion of Methicillin resistant Staphylococcus aureus (MRSA) isolates in participating countries in 2009. *Source*: EARS-Net

1.2 SOURCES FOR DRUG STATISTICS IN SWEDEN

- Diagnosis-Prescription Survey

Started in 1978. Gave outpatient data on diagnosis and treatment choices. Randomly selected physicians (around 30) were asked each week to participate in the survey for one week. The data could not be traced to a particular clinic, doctor or patient [18]. Participation was voluntary and due to low uptake – the survey was terminated in 2002. At that time electronic prescriptions had become common.

- Prescription Surveys

National prescription survey Sales on prescription from 1974 [19, 20]. The sample size of prescriptions has varied during the years. Since 1996 it has comprised 100% of sales excluding dose dispensed drugs. Since 1999 dose dispensed drugs were also included [21]. A new individual drug record was introduced in 2005 where name, personal identity number, date, drug, amount and dose is recorded and kept for 15 months. It also contains information about the identity and profession of the prescriber. It is mandatory, but consent has to be given to let the physician or pharmacy personnel have access to the record [22-23]. Since 2009, Apotekens Service, has had the legal responsibility to collect and distribute statistics on prescribed drugs in Sweden.

Jämtland survey Register on individual purchase of drugs by 1/7 of the population in the county of Jämtland (around 18 000 people). Data has been collected since 1970 [24].

Tierp survey started in 1971 and is based on the inhabitants in Tierp municipality (around 20 000 people). The database contains individual information on purchased prescribed drugs, but also on health care utilisation [25].

- Sales Statistics on Drugs has been available in Sweden since 1975 [21].

1.3 ANTIBIOTIC PRESCRIBING

In a global context, Sweden is a low-prescribing country with respect to antibiotics [6, 26]. Reliable data on sales statistics of antibiotics is available in Sweden [21, 27] and studies on antibiotic prescribing have been conducted in outpatient care [28-30]. In outpatient care, sales statistics has varied between different counties from 9.7 to 13.7 DDD per 1000 inhabitants and day in 2010 [27 and Appendix I]. In DDD per 1000 inhabitants and day, there has been a decrease in antibiotic sales in outpatients in all groups except for pivmecillinam, nitrofurantoin, isoxazolylpenicillins and trimethoprim-sulfonamides. PcV represents the highest proportion of all antibiotics prescribed in Sweden in outpatient care, followed by tetracyclines, figure 4.

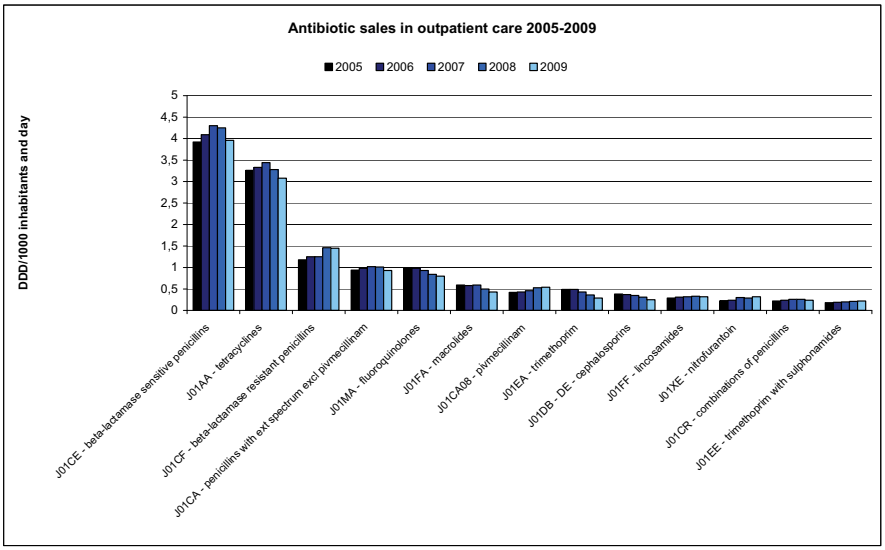


Figure 4. Antibiotic sales in outpatient care 2005-2009. *Source*: 2005-2008 Apoteket AB, Xplain Statistics. 2009-2010 Apotekens Service AB, Concise.

The sales for antibiotics commonly prescribed for RTI in outpatients are dominated by PcV, followed by doxycycline, figure 5. There is a wide variation of RTI-antibiotics within the country in number of prescriptions per 1000 inhabitants where it ranged from 146-258 in 2009 [31].

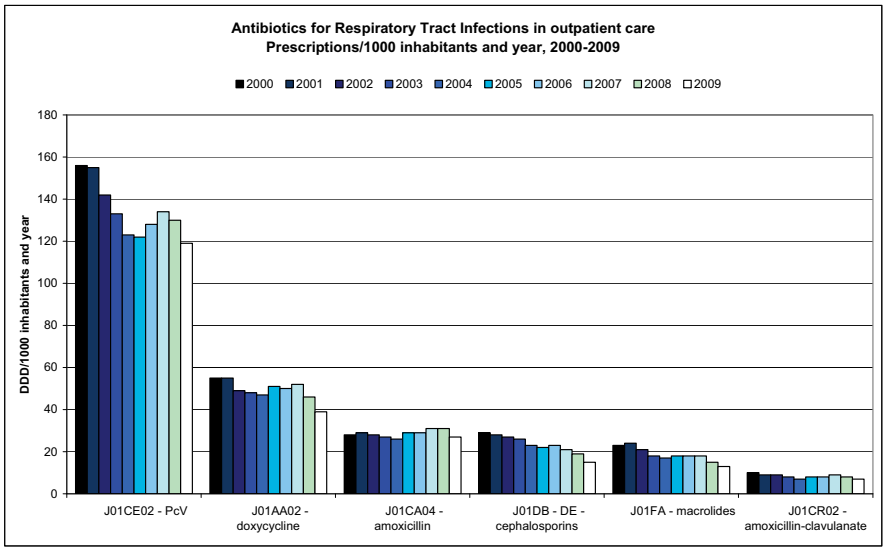


Figure 5. Antibiotic sales for respiratory tract infections in outpatient care between 2000-2009. *Source*: 2000-2008 Apoteket AB, Xplain Statistics. 2009 Apotekens Service AB, Concise.

Antibiotics commonly prescribed for UTIs in women show a trend towards less use of quinolones and trimethoprim in favour of an increase in pivmecillinam and nitrofurantoin, which is in line with current recommendations, figure 6.

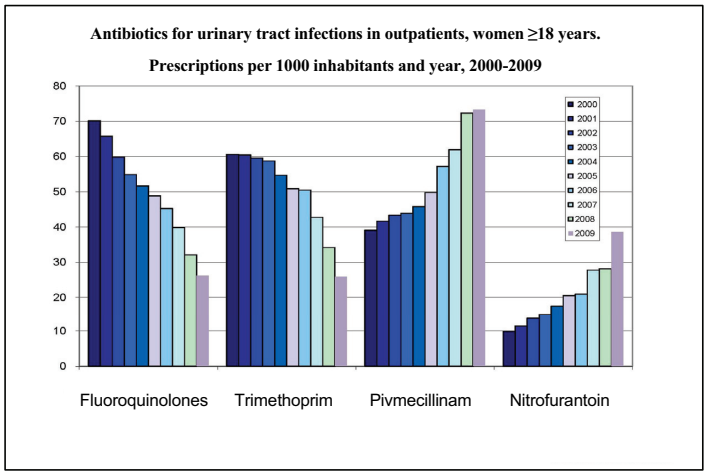


Figure 6. Antibiotics for urinary tract infections in outpatient care, women ≥18 years. Prescriptions per 1000 inhabitants and year between 2000-2009. *Source*: 2000-2008 Apoteket AB, Xplain Statistics. 2009-2010 Apotekens Service AB, Concise. Presented by Strama.

Thus, when this project started sales data for antibiotics and resistance patterns were available, but after the ending of the diagnosis prescription survey, detailed knowledge about treatment patterns for different diagnoses would not be available. Little was known about the prescribing process as well as on actual use, in particular concerning the institutionalized elderly. The National Board of Health and Welfare had called for action in this field [10].

1.4 A SHORT OVERVIEW OF AETIOLOGY, ANTIMICROBIAL SUSCEPTIBILITY AND RECOMMENDED THERAPY FOR PNEUMONIA, UTI AND SSTI.

All recommendations mentioned here are for empiric treatment in adults, without any complicating factors. Medical staff is referred to the original sources of recommendations for a complete picture.

1.4.1 Pneumonia

The most common pathogen causing pneumonia in both adults and elderly is *Streptococcus pneumoniae*. The distribution of pathogens in outpatients in Sweden and in hospital-based studies of elderly patients in different countries is described in table 1 below [32, 33].

Table 1. Reported frequencies of the most commonly isolated microorganisms for community acquired pneumonia, CAP, and nursing home acquired pneumonia, NHAP.

Pathogen	**CAP*** **(%)**	**CAP**† **(%)**	**NHAP**† **(%)**
Streptococcus pneumoniae	26	5-58	4-30
Haemophilus influenzae	17	2-14	0-2
Legionella pneumophilia	0	0-15	0-1
Mycoplasma pneumoniae	6	1-13	1
Chlamydia pneumoniae	3	0-28	0-18

*Lagerström *et al*. 2003. 82 patients with radiographically proven CAP and 95 patients without infiltrates in Sweden. Excluded patients <10 years, mean age 51 years (range 10-84 years) [32].
†Janssens and Krause 2004, Review [33].

The resistance rates for common antibiotics are low in Sweden both for *S. pneumoniae and H. influenzae,* figure 7 and 8.

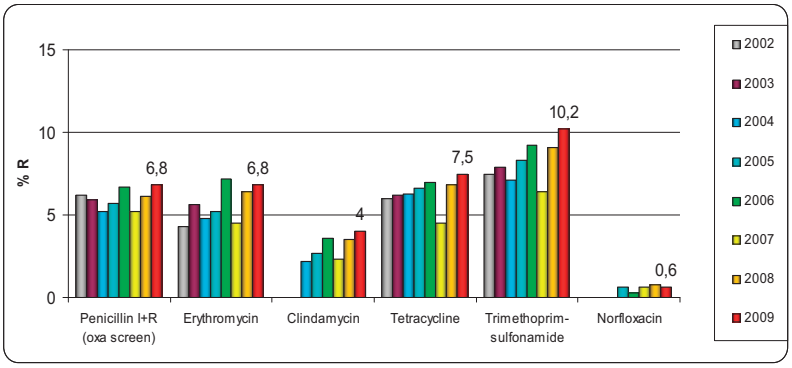
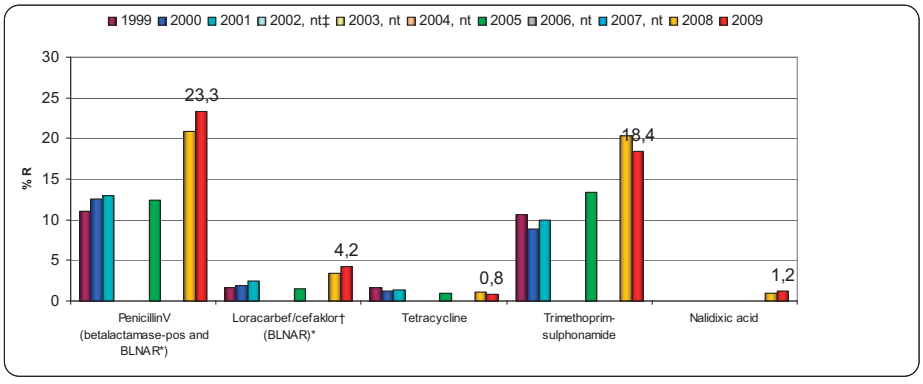


Figure 7. Resistance rates in *S. pneumoniae* 2002 - 2009. *Source*: Smittskyddsinstitutet (Swedish Institute for Communicable Disease Control).



* beta-lactamase negative ampicillin-resistant

† loracarbef 1999-2006, cefaklor 2007-2009

‡ nt, not tested

Figure 8. Resistance rates in *H. influenzae* 1999 - 2009. Nalidixic acid indicates quinolone resistance. *Source*: Smittskyddsinstitutet (Swedish Institute for Communicable Disease Control).

For empirical treatment of suspected pneumonia, PcV 1g x 3 for 7-10 days is the first-line choice. Doxycycline for 7 days (200 mg day one, and 100 mg the following days) is recommended if there is type I allergy to penicillins or therapy failure. If the patient has a chronic obstructive pulmonary disease, COPD, or other factors indicating *H. influenzae*, amoxicillin 500 mg x 3 or a tetracycline is recommended. Immunization against pneumococcal pneumonia and influenza is recommended for people ≥65 years of age and others with certain risk factors such as chronic pulmonary or cardiovascular diseases [34].

1.4.2 UTI

E. coli is the most common pathogen causing UTI in Sweden and abroad [35-37]. Opportunistic pathogens such as *Klebsiella spp*., *Proteus spp*. and enterococci are more frequent in the elderly, table 2.

Table 2. Distribution of pathogens in urine cultures.

Culture results	ECO.SENS (18-65 years)* % No. of cultures = 4734	Positive urine cultures in Kalmar and Växjö (≥65 years)† % No of cultures
Escherichia coli	53.3	47.0
Proteus mirabilis	4.4	5.5
Klebsiella spp.	2.2	7.5
Other Enterobacteriaceae	2.7	~ 4
Staphylococcus saprophyticus	2.5	0.4
Other pathogens‡	4.1	15 (enterococci =11)
Non-pathogens	18.9	15.5§
Negative culture	11.9	Only positive included

* Results from urine culture in the ECO.SENS study including women 15-65 years with symptoms of uncomplicated lower UTI in 16 European countries and Canada between Jan 1999 and Dec 2000 [35].

† Results from positive urine cultures from microbiology laboratories in Kalmar and Växjö, Sweden 1999 (should be mainly upper and complicated UTI, men included) [36].

‡ *Pseudomonas* spp. and enterococci.

§ Including *S. aureus* and *C. albicans*, which could be contamination, but they can in exceptional cases cause UTIs.

While the aetiology of lower UTI has not changed substantially over the years in different countries, the susceptibility pattern has changed. Therefore, in the new Swedish guidelines from 2007, trimethoprim was no longer considered a first-line choice in the empirical treatment of lower UTI in women. The first line choice of treatment needs to be reconsidered on a regular basis and thus local microbiology laboratories have an important role in providing updated information about the local resistance pattern. In long-term care facilities where urinary catheter is common (7%) and around 38 % had recently taken or were currently receiving antibiotics, opportunistic pathogens are more common [38, 39]. The resistance patterns in *E. coli* for common UTI-antibiotics in Sweden are presented in figure 9.

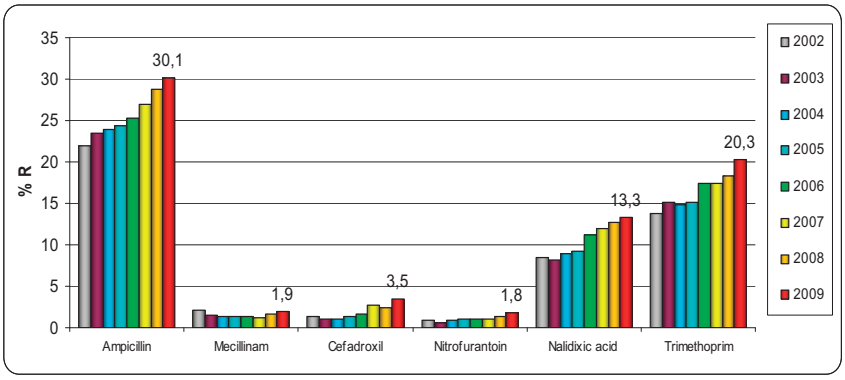


Figure 9. Resistance rates in *E. coli* 2002 - 2009. Nalidixic acid indicates quinolone resistance. *Source*: Smittskyddsinstitutet (Swedish Institute for Communicable Disease Control).

An overview of the recommended empirical choice of therapy for lower UTI in women is presented in table 3 [40].

Table 3. Recommended therapy for lower UTI in women.

Antibiotics	Dose	Treatment duration (days)
First-line therapy		
pivmecillinam	400 mg x 2	3*
	200 mg x 3	5
	200 mg x 2	7
nitrofurantoin	50 mg x 3	5
Second-line therapy		
trimethoprim	160 mg x 2	3
	300 mg x 1	3
cephadroxil	0,5 g x 2 el 1 g x 1	5
cephalexin	0,5 g x 2	5

* Women <50 years with sporadic lower UTI can be treated for three days, while women >50 should be treated for five to seven days. *Source:* Medical Products Agency – treatment recommendations for lower UTI in women, 2007 [40].

Treatment of UTI in men is different, and always seen as a complicated UTI as the prostate gland may be involved. Treatment choices are ciprofloxacin 500 mg x 2 or trimethoprim 160 mg x 2 or trimethoprim-sulfonamide 160/800 mg x 2 for 14 days.

1.4.3 Skin- and soft tissue infections

Staphylococcus aureus is the most common pathogen causing skin and soft tissue infections, SSTI, table 4 [41, 42].

Table 4. Pathogens in skin- and soft tissue infections

Pathogen	Primary SSTI*, n=119 %	SSTI†, n=6548 %
Staphylococcus aureus	60.5	53.6 (incl. CoNS§ 7.3 and MRSA‖ 0.3)
Staphylococcus lugdunensis	14.3	2.6
Enterobacteriaceae spp.	33.0	10.1
Anaerobic bacteria‡	16.0	10.5
Gram positives	5.9	6.3
Other	0	11

* Sjölund and Kahlmeter 2008, Sweden. Primary SSTI included, not secondary to e.g. trauma. For comparability the table only represents the 119 positive samples of the 175 samples taken from Nov 2006 to Apr 2007 with 78 males 97 females, mean age 43 years (range 1-99) [41].

† Medical products agency, Sweden. Isolates from inpatients and outpatients 2007. In recommendations for treatment of SSTI, 2009 [42].

‡ Including facultative anaerobic streptococci

§ coagulase-negative staphylococci

‖ Methicillin-resistant *Staphylococcus aureus*

The resistance rates in *S. aureus* are presented below in figure 10.

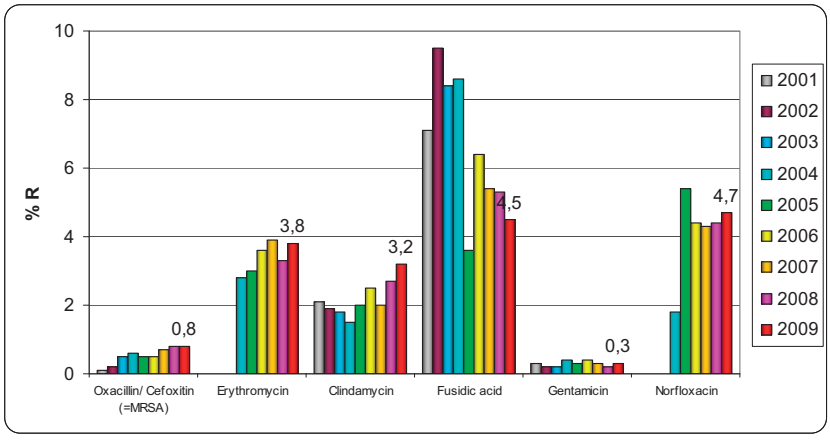


Figure 10. Resistance rates in *S. aureus* 2001 - 2009. *Source*: Smittskyddsinstitutet (Swedish Institute for Communicable Disease Control).

Antibiotic treatment for SSTI is generally only indicated for erysipelas or if the patient has a poor general condition, fever or disseminated infection. For empirical treatment of SSTIs suspected to be caused by *S. aureus*, isoxazolylpenicillin 750-1000 mg x 3 is recommended. In erysipelas, caused by group A streptococci, GAS, the recommended

treatment is PcV 1g x 3 for 10 days or if there is type I allergy to penicillins, clindamycine 300 mg x 3. Antibiotic treatment of hard-to-heal leg ulcers is seldom motivated if not GAS has been isolated or disseminated infection is suspected [42].

1.5 ANTIBIOTIC PRESCRIBING AND NURSING HOMES

The number of people living in special forms of housing in Sweden, including nursing homes, has decreased from 115 500 (7.5% of the population ≥65 years) in 2002 to 95 400 (5.7% of the population ≥65 years) in 2009 [43]. The exact number of special forms of housing for the elderly in Sweden is not known, but in 2008 the National Board of Health and Welfare estimated this number to 2596 [44]. Approximately 70% of those living in nursing homes are women and around 80% are 80 years or above [45]. Elderly people are often more susceptible to infections than the population in general. During the last decade, the elderly, ≥65 years, have had the highest prevalence of dispensed antibacterials for systemic use, with the exception of the age group 0-4 years [31]. Seasonal variation in antibiotic sales to the elderly over 80 years of age is low, which is illustrated in figure 11.

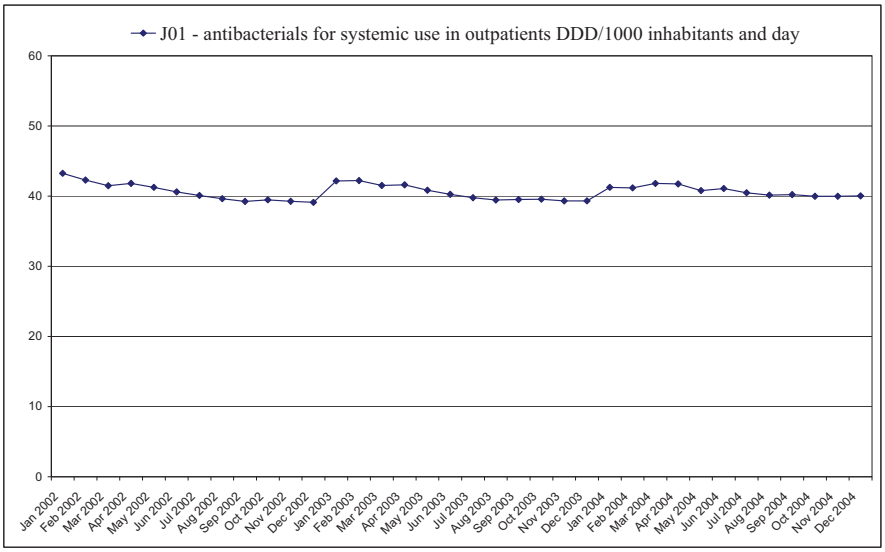


Figure 11. The sales of antibacterial drugs for systemic use in outpatient care for patients over 80 years of age. Prescriptions per 1000 inhabitants and month from January 2002 to December 2004. *Source*: Xplain-statistics, Apoteket AB.

The use of antibiotics is greater in women than in men, both in the elderly and in the population as a whole [27]. The most common indication for antibiotics in long-term care facilities is UTI [46-50]. Asymptomatic bacteriuria, ASB, is common in the elderly and in nursing homes a prevalence of 25-50% in women and 15-40% in men has been found [51, 52]. In Infectious Diseases Society of America guidelines, ASB is defined in asymptomatic women, as two consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts $\geq 10^5$ colony-forming units (cfu) per mL. For asymptomatic men, bacteriuria is defined as a single, clean-catch,

voided urine specimen with one bacterial species isolated in a quantitative count $\geq 10^5$ cfu/mL. For women and men, a single catheterized urine specimen with one bacterial species isolated in a quantitative count greater than or equal to10^2 cfu/mL defines bacteriuria [53]. In both women and men with long-term indwelling urinary catheters, almost all have bacteriuria [54]. In elderly, ASB is a benign condition [55, 56] which should generally not be treated with antibiotics [57].

Treatment of infections in the elderly requires well organised diagnostic measures and treatment guidelines as symptoms and signs of infection are usually indistinct and can appear as, for example, functional disorders such as confusion, falling or increasing incontinence [58, 59]. As a patient group, the elderly are vulnerable and generally have a high consumption of pharmaceuticals [60, 61]. Moreover, resistance rates are high in long-term care facilities [62]. The risk of Clostridium difficile associated disease, CDAD, is higher in nursing homes residents than others, due to advanced age, frequent hospitalisation and a high exposure to antibiotics [63]. In a nationwide study in 1995 the annual incidence of community associated CDAD in Sweden was median 20; range in different counties 5-47 per 100,000 inhabitants. The hospital associated CDAD was 27; range 17-51 per 100,000 bed-days [64]. As sales statistics of antibiotics showed a decrease in the population as a whole in Sweden since 1993, but an increase in people above 80 years of age, this further supported the need for studies on the use of antibiotics in the elderly [65]. Previously published studies on infections and antibiotic prescribing in Swedish nursing homes, have indicated a need for educational efforts on behalf of the nursing home personnel concerning infections [46, 47].

There were only a few studies on antibiotics in the Swedish context, which had focused on the situation for the institutionalised elderly. One of the problems with statistics on drug prescribing in nursing homes, is that some of the antibiotics are ordered for the nursing homes and not for an individual. To our knowledge there were three published studies that had described the indications for antibiotic use in nursing homes in Sweden when we started to plan for this project [46, 47, 66]. The problem was that they were relatively small and/or local, which made it difficult to generalise the results. However, their findings suggested that nursing homes should be of particular concern and pointed out a potential irrational use of quinolones [46]. Internationally there were also some studies concerning antibiotic use for nursing home residents [48-50, 67, 68]. Due to differences in health care and guidelines for antibiotic use, comparisons concerning treatment and recommendations are often difficult to make [47-49, 67]. In 2005 an intervention study in Canada and USA on antibiotic prescribing for suspected UTI in nursing home residents, was published with similar methodology to ours [69].

1.6 CHANGING PRESCRIBING BEHAVIOUR

Approaches to deal with problems in the prescribing of drugs and ways of influencing the prescribing behaviour have varied. For example, the National Board of Health and Welfare have been working on the development of quality indicators and criteria for drug use in the elderly [70]. Beers *et al.* 1997 have also developed criteria, but they define inappropriate medication rather than appropriate [71]. Another approach that has been used, is to gather local experts for their opinions, for example that authorities or

other organisations arrange consensus meetings with following dissemination of guidelines or the multidisciplinary drug reviews in nursing homes or [34, 40, 42, 53, 72].

Earlier studies have generally used the amount of pharmaceuticals (number of pharmaceuticals or the dose) as an indicator for rational prescribing and assumed "the lower the better" [73]. Our hypothesis was that the complex process of prescribing antibiotics requires more sophisticated methods to measure the quality, than simply assuming that a low consumption of antibiotics equals a high quality of prescribing.

Changing professional behaviour is a complex process, where theories of change as well as theories of continuing education need to be considered [74-76]. Prochaska's stages of change model postulates that people are in five different stages based on their readiness to change: precontemplation, contemplation, preparation, action and maintenance [77]. These stages of change are part of the transtheoretical model, which offers a framework for understanding and intervening in human behavioural change. The other two parts being process of change and level of change [78]. Initially its main application was within the area of addictive behaviours. However, more recently it has been suggested for tailoring interventions for continuing medical education [79, 80]. Shirazi *et al.* 2009 used a modified Prochaska model where the stages were reduced to three: attitude, intention and action [81, 82]. The results suggest that the modified Prochaska model could be used for improving general practitioners' skills in management of depressive disorders. Basically what the Prochaska model would suggest in our context is that a successful intervention must first assess the stages of readiness to change in which the participants are situated and provide means to assist them from one stage to another and thus promote change.

Experience from the USA suggests that sustainable changes have to involve the physician and the nurse responsible for the patient, and that information exchange and changes in behaviour are most easily achieved through meetings between people [83-86]. There are also results from Sweden that encourage multidisciplinary team interventions [87, 88]. Social and behavioural science has provided us with theories and helpful information on how to change behaviour and thus develop successful interventions [89, 90]. Systematic reviews on changing professional practice, suggest that a combination of intervention strategies is crucial for successful results [91-95]. A Cochrane review, concerning improvement of antibiotic prescribing, points out that the selection of a successful intervention is condition and situation specific. Although cautious in their conclusions, they suggest that more complex intervention strategies in general seem to be more effective than simple approaches, such as distribution of guidelines only, didactic educational meetings, and audit and feedback [96]. According to a review in 2006 the effect that could be expected for an intervention targeting antibiotic treatment, is around the magnitude of 10%. Addressing the treatment decision, including 34 studies, mostly respiratory tract infections, RTI median: -8.9% (interquartile range (IQR) -12.4% to -6.7%) and those addressing the antibiotic selection decision (26 studies, RTI or UTI) median 10.6% (IQR 3.4% to 18.2%) [97].

The diagnosis-prescription survey had provided information on the percentage of patients with infectious symptoms that were prescribed an antibiotic and the indication

for specific antibiotics. But problems with this survey had been a low uptake, and that the results could not be traced to a certain clinic, doctor or patient, thus making it difficult to evaluate and improve the prescribing pattern where necessary. A complement to the diagnosis-prescription survey was needed. Since 2005 the national prescription database has contained all prescription-drugs dispensed at the pharmacy. However, the indication is not registered.

The increase in antibiotic prescription for the elderly and the lack of national studies in the area, were the main reasons for initiating the study, which we refer to as the Swedish Antibiotic Nursing home Trial (SANT). It was a collaborative project between Karolinska Institutet, Strama (The Swedish Strategic Programme for the Rational use of Antimicrobial Agents) [11, 12] and Apoteket AB (The national corporation of Swedish pharmacies). In addition, the study was linked to an EU-funded project "A framework and tools to develop effective quality improvement programmes in European healthcare" (QLRT-2001-00657), where quality improvement projects from seven countries were linked together in order to build on the complementary strength of the partners. This randomised controlled intervention study falls within the area of pharmacoepidemiological intervention studies. The overall aim of SANT was to describe the prescribing of antibiotics in nursing homes for the elderly, and to develop and evaluate an educational intervention, targeting physicians and nurses working in nursing homes, as a means of quality improvement with regard to prevention and treatment of infections. The major part of this thesis project employs data derived from the SANT-study.

To elucidate different aspects of the treatment of infectious diseases in the institutionalised elderly in a health system's research perspective, we found interdisciplinary work important, thus researchers with several professional backgrounds were included in the study group.

The term "special forms of housing" has been debated in Sweden and according to Lennarth Johansson, 2002, at the elderly unit of the National Board of Health and Welfare, this is more than an academic problem. The confusion of concepts leads to difficulties in comparing municipality care, causes problems in the work of the regulatory authorities and also affects the legal security of the residents [98 and personal communication 2011]. The term nursing home is in this thesis used for special forms of housing for the elderly where the residents have common health care personnel and have the opportunity to eat in a common dining room.

2 AIM AND OBJECTIVE OF THE THESIS

2.1 MAIN AIM AND OBJECTIVE

The aim was to present the treatment of infections in outpatients and in the elderly in nursing homes, and further to develop and evaluate the effect of an educational intervention aiming at improving treatment with antibiotics in Swedish nursing homes.

2.2 SPECIFIC OBJECTIVES

The specific objectives were to:

- Present the treatment patterns regarding infectious diseases in outpatients (I) and elderly residents in nursing homes (II).
- Through focus group discussions and collection of knowledge- and attitude data, elucidate the decision making process for antibiotic prescribing in nursing homes (III), target the intervention and explore barriers and facilitators for behavioural change.
- Evaluate the effect of the intervention on quantity and quality of prescribing in relation to available guidelines (IV)

3 MATERIAL AND METHODS

3.1 STUDY OUTLINE

3.1.1 Outpatient study

A cross-sectional study conducted during one week in November 2000, where outpatient diagnosis-prescribing data was analysed in five different counties in Sweden.

3.1.2 Swedish Antibiotic Nursing home Trial - SANT

Phase 0: Pilot study and focus group discussions
Phase I: Baseline study i.e diagnosis-prescribing study (DPS) nursing home questionnaire (NHQ) and knowledge and attitude (KA) -survey
Phase II: Educational intervention
Phase III: Post intervention DPS, NHQ, KA and evaluation

The intervention study was the first major study, focusing on antibiotic use and methods for improvement in the institutionalised elderly, which included a wide variety of locations in Sweden. Interdisciplinary work and evaluation of the methods in the pilot study were measures taken to increase the use of the method outside the research setting as well as to increase the likelihood of sustainable changes. A time frame for SANT is presented in figure 12.

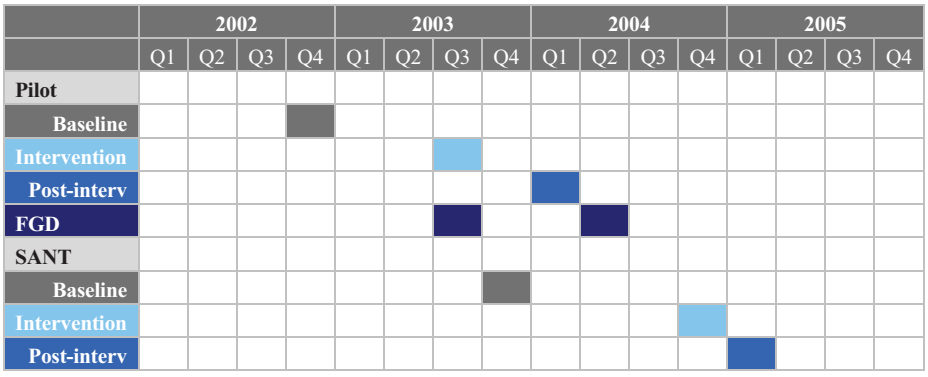


Figure 12. Time frame for when the different phases were conducted in the Swedish Antibiotic Nursing home Trial – SANT.

3.2 STUDY DESIGN

A summary of study designs that has been used in the four different papers that this thesis is based on is presented in table 5.

Table 5. Summary of main study designs used

	Paper I	Paper II	Paper III	Paper IV
Study designs used	Cross-sectional	Cross-sectional	Mixed methods Focus group discussions and Cross-sectional	Randomised controlled trial, RCT

Cross-sectional studies, which are the chosen design for paper I and II are observational studies i.e the researcher only measures what is there, without intervening. The advantages are that they are simple and cheap in comparison to more complex experimental design and they provide individual data, which ecological studies with aggregated data are unable to offer.

A mixed methods design was chosen for Paper III. Mixed methods research has been defined by Tashakkori and Creswell 2007, as "research in which the investigator collects and analyses data, integrates the findings, and draws inferences using both qualitative and quantitative approaches or methods in a single study or a program of inquiry" [99]. The use of mixed methods has been the cause of some debate in social science. According to Onwuegbuzie and Teddlie, 2003 there can be advantages to combining methods at a chosen level [100]. The presentation of mixed methods can be challenging, but Östlund *et al.* 2011 is of the opinion that mixed methods and triangulation is also helpful within nursing and health care sciences to clarify, understand, and draw valid conclusions from the result [101].

The rationale for choosing focus group discussions was mainly based on the objective of Paper III. Focus groups provide the unique opportunity to capture interaction between the participants [102, 103]. As we wanted to study shared experiences we chose homogenous groups i.e we divided the participants into groups comprising nursing assistants, nurses and general practitioners. EP was the facilitator at all focus group discussions. We used a semi-structured guide with exploratory probe questions to be used if the discussion faltered. The main items were "infections and the elderly", "difficulties in treating UTI in the elderly", "hygiene", "management of infections – anything you wish to change in your nursing home?" and "advice for development of an education concerning infections". The focus group discussions were tape-recorded and transcribed. The data was analysed using content analysis influenced by the five different stages in the framework model [104]. 1) Familiarisation was achieved by listening to the tapes, reading the whole transcripts and the observational notes several times and by making notes in the material 2) A thematic framework was identified by noting key issues and referring to the aims that were set at the beginning of the study 3) All the data was Indexed by noting parts with the same content in the margin 4) The step referred to as Charting was made by cutting, pasting and coloring the parts with similar content that was indexed in the previous stage from different FGDs. This part is

a form of decontextualisation. 5) In the last stage, mapping and interpretation the data was recontextualised and once again interpreted as a whole while keeping the aim in mind. The theme that emerged came from reading the transcripts interpretively over and over again and looking for an essence in the material [105].

The SANT-trial is a cluster randomised controlled intervention study with two study arms i.e intervention and control group. For guideline implementation studies, the cluster randomised controlled trial is considered to be the optimal design [74]. It has advantages such as lowering the risk of contamination in comparison with patient randomised controlled trials. However, the statistical power is reduced compared to a patient randomised trial of equivalent size [106]. The assumption of the data being independent is also altered in cluster randomised trials, so certain steps need to be taken in the planning and analysis of the study [107]. Patients, or in this case the targets of our intervention - nurses and physicians within one cluster - are more likely to respond in a similar manner to the intervention. This intracluster dependence is taken into consideration by calculating the ICC, Intracluster Correlation Coefficient or using estimates of ICC from the literature [106].

3.3 STUDY POPULATION AND SETTING

3.3.1 Outpatient study

During one week in November 2000 five counties: Uppsala, Östergötland, Kronoberg, Dalarna and Jämtland participated in this prospective study where all patients with an infectious complaint were registered regardless of whether they were prescribed an antibiotic or not. The counties were selected to generate a geographic spread, and to include both high and low prescribing counties. The sales of antibacterials for systemic use in 1999 ranged from 12.7-16.5 DDD/TIND in the selected counties [27]. 155 primary care centres (~ 600 doctors), 24 hospital departments or specialised surgeries (ears, nose, throat - ENT, infectious diseases and paediatrics) and 20 individual private practitioners agreed to participate.

3.3.2 Pilot study and SANT

Inclusion criteria for participating nursing homes in the SANT-trial were nursing homes or special types of housing where the facilities included a common dining room and common health personnel. To reduce the number of drop-outs it was desirable that staff turnover was low and that the nursing home had a contact person available. Specialised nursing home/wards e.g. oncology wards were not included in the study.

The pilot study took place in the county of Norrbotten and the subsequent phases in different parts of Sweden, see also table 6.

All registered nurses charged with the medical responsibility for nursing homes in Sweden were invited (n=366, at the time of invitation) to participate in the study. Those who took an interest in the study forwarded the information to the nurses at the nursing homes in their area, who then decided whether or not to participate. Participation was voluntary and based on the participants' willingness to co-operate.

3.3.2.1 Sample size for SANT

The following assumptions have been made. At least 25% of the residents will have an infection during the three months of data collection, according to the pilot study (27-34%). At least 90% (90-98%) of these will receive antibiotics. During the baseline of the pilot study, 4.9% of the residents received a quinolone. In another study there were 4.7% quinolone users [46]. To cover both, the quinolone users were assumed to be between 4.5% and 5.5%. The intracluster correlation coefficient, ICC, was assumed to be 0.05. In another study similar to ours, the ICC was 0.04 [108]. Standard sample size calculations need to be inflated by a factor known as the design effect, Deff = 1 + (n – 1) ρ; where n is the average cluster size and ρ is an estimate of the ICC [109].

The following figures were included in the power calculations:

- ICC was given the conservative value of 0.05
- Weighted average number of residents in each nursing home was 60
- Deff, was calculated to 3.94
- Level of significance was set to 0.05
- Power: 80% and 90% respectively.
- The least difference we wanted to be able to detect was 20% related to the use of quinolones in the control group.

With 80% power we needed 863-1121 in each study arm (5.5% - 4.5% quinolone users) and with 90% power we needed 1159-1498 in each study arm.

65 nursing homes were eligible for participation at the start of SANT.

3.3.3 Focus group discussions

The participants in the focus group discussions were recruited separately from the pilot study and SANT-trial. The participants were selected purposively to represent different categories of staff working in nursing homes i.e nursing assistants, nurses and GPs. As one purpose of the focus groups was to share and discuss about experiences of infections in the nursing home setting, the participants needed to have some own practical experience from working in nursing homes. The nursing assistants and nurses came from Norrbotten county and the general practitioners from Jönköping county.

The study was conducted at the division of Global Health (IHCAR) at the Department of Public Health Sciences, Karolinska Institutet in collaboration with the hospital pharmacy in Sunderbyn.

3.4 PHASE 0: PILOT STUDY AND FOCUS GROUP DISCUSSIONS

The pilot nursing homes took part in a small-scale study, without a control group i.e a before and after study. Medical Responsible Nurses in two municipalities in Norrbotten county were contacted and informed about the project. Interested nursing homes were invited to participate in the pilot project. The aim of the pilot study was to:

- Develop the instruments to be used in the SANT-trial (DPS, KA, NHQ, educational intervention and evaluation form)
- Estimate data collection time needed for the diagnosis prescribing survey in order to achieve a sufficient number of observations.

- Test the questionnaires, which were used during the nursing home and knowledge and attitude survey, for feasibility and face validity.
- Adjust the way of working in order to increase the feasibility.

The focus group discussions have been used as a tool to understand the prescribing process of antibiotics and target the need for continuing education and explore barriers and facilitators for behavioural change.

3.4.1 Development of the instruments for outcome measurements

The instruments for outcome measurements were developed through several meetings and correspondence with other members of the research group. They were thereafter tested and discussed during the pilot study. The three main outcome instruments are described below.

The form used for the DPS, was a modified version of the form used for studying antibiotic prescribing in out-patients [Paper I]. As the form had been used in another setting, the content of the questionnaire was modified to suite the infection pattern in the nursing home setting.

The main content of the NHQ was resident and nursing home characteristics such as number, age, sex and functional status of the residents and human resources. Later on it also included questions concerning infection control routines and number of residents immunised against influenza. It gave us basic information about all the included nursing homes and was also to be used in comparison and explanation of the results between the different nursing homes.

The KA-form was developed during project group meetings, mainly based on experience from the members in the project group and the literature. The focus was on treatment and management of UTI. It also contained fictitious cases of UTI. The fictitious cases are modified versions of the fictitious cases developed by IHCAR (Stålsby Lundborg C and Wahlström R) and Strama during the "Year of infection, 2000" (for each year Apoteket AB, The National Corporation of Swedish Pharmacies, had a special theme).

3.4.2 Changes in the instruments for outcome measurements

Some changes in the questionnaires were made before the main trial. For the DPS questionnaire the indications for SSTI were extended and the indications for respiratory tract infections were reduced. Questions about earlier infections and use of antibiotics during the last three months were added. The question on where the antibiotics were retrieved from was excluded and the order of the questions was rearranged. In the pilot study the same KA-questionnaire was used for physicians and nurses. In the main study different questionnaires for physicians and nurses were used. The items concerning the choice of treatment were reduced in the nurses' questionnaire. Before the main trial, the NHQ was extended to also include questions concerning hygiene and vaccination with influenza vaccine.

The questionnaires used in the main trial (DPS and KA have been translated from Swedish to English) can be found in Appendix II (DPS), III (NHQ), IV (KA physicians) and V (KA nurses).

3.4.3 Outcome measurements

The outcome measurements were set based on experiences from paper I, further analysis of data concerning the elderly of data collected for paper I, the pilot study and project group meetings.

3.4.3.1 Primary outcome

Proportion of quinolones prescribed for lower urinary tract infection, UTI, in women.

3.4.3.2 Secondary outcomes

For all infections

i. proportion of recorded infections treated with an antibiotic
ii. proportion of infections handled by "wait and see" by the physicians

For lower UTI in women

iii. proportion of nitrofurantoin

3.4.4 Development of the intervention

As a process evaluation tool or checklist to describe the intervention, the framework for describing the key features of a quality improvement intervention published by Hulscher *et al.* 2003, has been used [110]. To identify barriers and facilitators and to be able to tailor the intervention to the target group, we used: literature search, multidisciplinary project meetings, focus group discussions, baseline data and eventually also the experience acquired during the educational intervention in the pilot study. The focus group discussions were for feasibility reasons not fully analysed before the intervention. However, the facilitator for the focus group discussions and the intervention was the author of the thesis, and thus the experiences from the focus group discussions could be brought into the educational sessions. During the development of the intervention, several project meetings were held where the questionnaires and methods were discussed. The project group was multidisciplinary and had vast experience from the areas of infection, hygiene, statistics, social science, pharmacy, pharmacology, intervention studies and experience from working in nursing homes. In Appendix VI there is an overview of how the different parts of the thesis project contributed to the intervention.

3.4.5 Description of the intervention

3.4.5.1 Main components and content of the intervention

Two parts of voluntary *continuing medical education* of 1.5 hours each. The facilitators were one pharmacist (EP), one physician and one hygiene nurse if available. The physician was an infectious disease specialist (sometimes the head of communicable

disease control in the county) or general practitioner with experience from Strama work. The facilitators presented the *educational material*.

Part I consisted of results from the baseline data collection and local resistance and prescribing pattern was discussed. During this session the prescribers got *feedback* on their prescribing.

Part II was a presentation of guidelines for treating UTI, pneumonia and skin- and soft tissue infections. It also contained information about immunization against influenza and pneumococci. The facilitators encouraged a discussion on the presented information and introduced some important questions that we wanted to have addressed during the sessions. Routines for influenza vaccination and what had been done locally to increase the number of immunised residents, was for instance part of the presented material. A hygiene leaflet was distributed during the discussion on hygiene in the nursing homes. As a *reminder* from the education session, a verbal summary was made and a short written guideline for antibiotic prescribing was distributed at the end of part II.

The educational material used, including references, cannot be found as an appendix to this thesis as it is in Swedish, but can be requested at no-cost from Eva Pettersson by sending an e-mail to eva.pettersson@ki.se or eva.e.pettersson@apoteketfarmaci.se Note that the guidelines have been changed. For example trimethoprim is no longer a first-line choice for treatment of lower UTI in women.

3.4.5.2 Target group of the intervention

Nurses and physicians (usually general practitioners, GPs) connected to the intervention nursing homes were invited to participate in the intervention.

3.4.5.3 Main outcome measures

See separate section 3.4.3

3.4.5.4 Evaluation of the intervention

After education part I and II respectively, a written evaluation was done using a questionnaire with a six-point Likert scale, Appendix VII.

3.4.5.5 Guidelines

The acknowledged guidelines for the study were mainly based on available national and/or regional recommendations and material at the time for the study from Strama, Swedish Medical Products Agency, Apoteket AB, Svenska infektionsläkarföreningen (Swedish Association for specialists in infectious diseases) and the local drug therapeutic committees. In Sweden at the time for the intervention, the recommended antibiotics for lower UTI in women were pivmecillinam, nitrofurantoin or a cephalosporin for 5-7 days, or trimethoprim for 3-5 days. For pneumonia, considering the aetiology, penicillin V should have been the most prescribed antibiotic followed by amoxicillin.

3.4.5.6 Barriers and facilitators for changing professional behaviour

Obvious factors that could affect the study results negatively were if the participants found it too time consuming to fill in the registration form or if too few were exposed to the intervention. This was already being taken into careful consideration at the planning stage of the study. The form used for the DPS in the SANT-trial had been used earlier in registration of infections in outpatients, where it had already been evaluated [Paper I]. However, as it was modified for this patient group and setting, we needed to re-evaluate it in the pilot study.

Identified barriers and facilitators to change that were applicable in our study were:
- Knowledge about guidelines
- Attitudes toward the specific guidelines and guidelines in general
- Social factors, such as opinion leaders and colleagues at the nursing home/health care centre
- Organisational factors including availability of guidelines at workplace and availability of antibiotics.
- Structural factors such as location and building.
- Economic factors such as lack of resources (time, personnel).

The intervention mainly addressed the first four barriers/facilitators. The study design took economic factors into account, to the extent that the forms used were simple and quick to complete and the intervention was offered several times so that staffing issues could be solved. However no part of the intervention in itself dealt with economic factors.

3.5 PHASE I: BASELINE STUDY, DIAGNOSIS-PRESCRIBING STUDY

The baseline data collection was conducted during three months from the 15th of September 2003 to the 15th of December 2003. Baseline data collection consisted of three parts: a diagnosis-prescribing survey (DPS), a nursing home questionnaire (NHQ) and a knowledge and attitude survey (KA), see Appendix II, III, IV and V.

For the DPS, Appendix II, the responsible nurse was requested to fill in a form for all patients with infectious symptoms which required a physician's opinion. Recorded information included patient data, duration of symptoms, and kind of contact with physician (direct or indirect contact), the main diagnosis, diagnostics, treatment with antibiotics, referral or both, type of antibiotic and treatment length and factors influencing the choice of treatment. The form is a slightly modified version of the one previously used in the outpatient study in Paper I.

The NHQ, Appendix III, was used to collect information about the nursing homes, such as human resources (recalculated as full-time employees), availability of doctors (number of hours per week) infection control routines, age and gender of the residents, number of residents immunised against influenza, functional status of the residents etc.

A knowledge and attitudes (KA) questionnaire was sent to participating physicians, Appendix IV and nurses, Appendix V. It included questions on management and treatment of UTI and also fictitious UTI cases.

3.6 RANDOM ASSIGNMENT

After the collection of baseline data (phase I) the nursing homes were randomly assigned (i.e randomisation was done at nursing home level) to control or intervention. As one of the aims of the intervention was to decrease the number of diagnosed UTI/residents, we decided to stratify the material into 3 equally sized groups based on number of UTI/residents for each nursing home. To get a geographic spread of the intervention and control, the nursing homes were also divided into north, central and south Sweden (there are 3 defined regions called Norrland, Svealand and Götaland). The nursing homes within each of the nine final strata were randomly allocated to either intervention or control. This was done in SPSS. As the material was small, 9 different files were created in SPSS and then 50 % were selected randomly, with those selected belonging to the intervention group. For number of nursing homes in each study arm in the different counties, see table 6.

Table 6. Nursing homes in each study arm in the different counties.

County	Intervention	Control
Norrbotten	1	4
Västernorrland	1	0
Jämtland	3	2
Gävleborg	3	1
Dalarna	5	1
Värmland	3	4
Västmanland	4	3
Stockholm	2	6
Södermanland	1	0
Örebro	0	1
Jönköping	0	1
Västra Götaland	0	1
Kalmar	2	2
Kronoberg	0	1
Skåne	4	2
Total	**29**	**29**

3.7 PHASE II: EDUCATIONAL INTERVENTION

The nursing homes in the intervention arm received the educational intervention from the 25th of October 2004 to the 21st of January 2005. Although it was considered that the peer group had considerable knowledge, we chose to have external facilitators during the educational sessions in order to take the discussions further and to introduce new material. A pharmacist together with a physician and a hygiene nurse were facilitators during the educational sessions. There were two sessions of approximately 1.5 hours each. An essential element was feedback on baseline results (phase I) and group discussions around them in relation to treatment recommendations, focusing on the major infectious disease areas, UTIs, pneumonia, and skin and soft tissue infections.

In addition to feedback and references to available guidelines, barriers to change such as structural, organisational and social factors were discussed. In order to standardise the intervention, material for presentation was developed and produced in the study group. The pharmacist i.e the author of the thesis was the same for all educational sessions. However, as we believed that a sustainable change would be more likely if we tailored the intervention for the different nursing homes, the participating physician and hygiene nurse were local and we referred to guidelines from respective drug therapeutic committee.

3.8 PHASE III: POST INTERVENTION DIAGNOSIS-PRESCRIBING STUDY AND EVALUATION

The post intervention data collection was undertaken from the 14th of February 2005 to the 16th of May 2005. Phase I, i.e. DPS, NHQ and KA were repeated for the nursing homes and the results were compared with the baseline results. As seasonal variations of infections (based on sales statistics) are small in this patient group, the months for the data collection were selected for practical reasons rather than in consideration of the infectious disease panorama (figure 11).

The intervention was evaluated and the feasibility of the method was assessed both by looking at the results from the post-intervention data and by questionnaires distributed to participating doctors and nurses. Appreciation was evaluated by a modified version of a questionnaire used earlier, Appendix VII [111].

Traditionally cluster randomised studies have used the cluster as a unit of analysis with only one aggregated data point per cluster. However, by using more complex approaches such as regression analysis or hierarchical models, patient level data may also be taken into account. Such approaches have been used previously [112].

3.9 DATA ANALYSIS AND STATISTICS

See also sample size calculations, section *3.3.2.1*. The software SPSS version 10.0 to 17.0 was used in the analysis of the quantitative data. For precision of measurements, the 95% confidence interval, CI, for proportions has been calculated. For, lower UTI in women, the major indication for antibiotics, the choice of antibiotics and duration of treatment was also assessed in relation to the recommendations. All figures describing the intervention effect have been adjusted for the design effect. After the intervention the ICC and the design effect was calculated for each outcome variable. For the primary outcome proportion of quinolones for lower UTI in women, the calculated ICC was 0.03. Deff = $1 + (n - 1)\rho$, where ρ is the estimate of ICC [109]. All standard errors for calculating the confidence intervals were adjusted for the design effect. To explore potential confounders a multivariable linear regression was performed in SPSS 17.0. The potential confounders explored were: residents' age, availability of physicians, nurses and nursing assistants, IUC, volume of disinfection alcohol consumed and special needs of the residents. The special needs of the residents were calculated as $1/7 \times Hyg_{prop} + 1/7 \times Cloth_{prop} + 1/7 \times Mov_{prop} + 1/7 \times Toi_{prop} + 1/7 \times Eat_{prop} + 1/7 \times Press_{prop} + 1/7 \times Leg_{Prop}$. Hyg_{prop} is the proportion of residents not managing personal hygiene. $Cloth_{prop}$ is the proportion of residents not managing clothing. Mov_{prop} is the proportion of residents not managing moving around. Toi_{prop} is the proportion of residents not

managing visits to the toilet. Eat_{prop} is the proportion of residents not managing eating. $Press_{prop}$ is the proportion of residents at the nursing home with pressure wounds. Leg_{Prop} is the proportion of residents at the nursing home with leg ulcerations. The choice of items in the special needs formula was influenced by Katz ADL-score. We chose to dichotomise the variables to either dependent or independent [113]

3.10 ETHICAL CONSIDERATIONS

Prior to the initiation of the project, ethical approval from the Ethics committee at the Karolinska Institutet and from local ethics committees was applied for and granted. Approval from the Ethical Committee in Umeå for the pilot study, (dnr 02-330) and approval from the Ethical Committee at Karolinska Institutet for the main study (including the focus groups, dnr 03-070) and for the analysis of diagnosis/prescribing data (dnr 03-280).

The head of all units involved in the project as well as involved physicians and nurses were asked to give their written informed consent.

The participation was voluntary i.e. only nursing homes where the doctors and nurses agreed to participate were included. The control nursing homes were also invited to an educational session, including feedback on data, after the post-intervention data collection.

4 RESULTS

4.1 THE PILOT STUDY

Seven nursing homes in two municipalities in Norrbotten county with a total of 472 residents (range 48-93, mean 67) and an average age of 84 years, were enrolled in the pilot study.

The results from the KA-questionnaire have mainly been used to target problem areas to be discussed during the intervention. Some lack of knowledge, or problem areas could be seen in diagnostics, symptoms of infection, IUC, when to initiate antibiotic treatment, duration of treatment, choice of treatment and gender differences in treatment. The results from the KA-questionnaire revealed a quite positive attitude towards quinolones whereas nitrofurantoin had a bad reputation for treatment in the elderly.

During the baseline of the pilot study, 4.9% of the residents received a quinolone. This figure was used in the sample size calculation for SANT (*3.3.2.1*).

From the DPS it was found that the average age of residents with an infection was 85 years. An overall decrease in total number of infections could be seen after the intervention – from 162 to 122. However, the number of infections related to the number of residents during the three-month data-collection at the different nursing homes ranged from 0.23-0.46 pre and 0.12-0.40 post intervention. At baseline, 90% were treated with antibiotics and post intervention this figure was 98%. The most common infection was UTI, in particular lower UTI, followed by skin- and soft tissue

infections and respiratory tract infections, RTI, where pneumonia was the dominating diagnosis. The proportion of short term regimens (≤5 days) increased from 3% to 25% after the intervention. In 52% pre and in 78 % post intervention in the pilot study, the antibiotics were retrieved from the medical supply room at the nursing homes and not by prescription.

The questionnaires were tested for face validity.

4.2 PAPER I

Paper I provided information about treatment of infections in outpatients. 7,029 of the 7,071 forms returned, included information on diagnosis; infections of the respiratory tract, urinary tract and the skin or soft tissues were responsible for 70%, 14% and 10% of the visits. In 59% of all cases antibiotics were prescribed. PcV was the most commonly prescribed antibiotic. Quinolones were used in 21% of females where a lower UTI was reported as the indication for antibiotics, where it is not the recommended choice of treatment. In conclusion, this study provided information on the treatment pattern associated with various infections.

The data collected for Paper I was further analysed comparing the elderly ≥ 65 with the group 16-64 years (unpublished results) and we found a significantly higher frequency of UTI, recurrent UTI and upper UTI in the elderly, and low prescribing of nitrofurantoin to the elderly. From this knowledge about infections in outpatients, the focus was directed towards the nursing homes, where it was known that UTI is a common infection [46-50]. UTI was to a large extent treated with quinolones in outpatients and we thus expected to find problem areas of antibiotic prescribing in the nursing homes.

4.3 PAPER II

This cross-sectional study based on data from baseline measurements in the SANT-trial provided us with information about the treatment pattern of infections in the nursing home setting. As expected a high proportion of the 889 registered infections were treated with antibiotics – 84%. The physician was often not present at the nursing home, but prescribed antibiotics on second hand information from the nurses e.g. by phone in 38% of the cases. The indication for antibiotics was in more than half of the cases an UTI. Treatment was in many cases not according to the guidelines. For example women with lower UTI received treatment which, in half of the cases, was not in line with the recommendations. The main concerns that we needed to focus on in the intervention were the high use of quinolones and the length of treatment. For pneumonia, the use of doxycycline needed to be discussed. The results from Paper II also supported the inclusion of both physicians and nurses in the educational intervention due to the high proportion of antibiotics reported to be prescribed without the physician being present at the nursing home.

4.4 PAPER III

The theme that emerged was: “Interpersonal relations, timing and setting – the main determinants for management of UTIs and antibiotic prescribing in nursing homes.” The focus group discussions provided a deeper understanding of the interplay between the

staff at the nursing homes and how it affects different important aspects in the prescribing process of antibiotics. The categories that appeared during the analysis were:

- Symptoms of urinary tract infections – clinical signs and attitudes
- What leads to antibiotic prescribing?
- What does a positive dipstick or positive urine culture mean?
- Communication between staff concerning infectious symptoms
- Hygiene in the nursing home setting

Although not included in the results section of paper III, one of the most important contributions concerning barriers and facilitators for behavioural change, which could not be elucidated from the pilot study, was the discussions and examples given on communication in the nursing homes. The praxis for communication seemed to differ between the nursing homes due to the people involved in the process. Another important input from the focus groups discussions regarding barriers and facilitators, was the addition of the nursing assistants' perspective. The structural and organisational barriers, especially difficulties of complying with hygiene guidelines were described both with examples of the different tasks of the nursing assistants and also availability of correct work wear such as disposable aprons and gloves.

4.5 PAPER IV

46 of the included 58 nursing homes completed the study. Pre and post-intervention, 702 and 540 infectious episodes respectively, were recorded. The effect on the primary outcome, proportion of quinolones prescribed for lower UTI in women, was not signficant 0.028 (95% CI -0.193 to 0.249). However, the proportion of infections treated with an antibiotic, decreased significantly in the intervention group, by -0.124 (95% CI -0.228 to -0.019), in comparison with the control group. The proportion of infections handled by physicians' "wait and see" policy, increased in the intervention group by 0.143 (95%CI 0.047 to 0.240) in comparison with the control group. We could not attribute an effect to the intervention on any of the other outcomes.

Both the intervention and the control group increased their adherence to the guidelines concerning the selection of antibiotics by 0.222 (95%CI 0.115 to 0.329) and 0.225 (95%CI 0.090 to 0.359) (not published results).

Out of the participants 164 were exposed to the educational intervention according to the attendance lists of which 13 were general practitioners. 165 nurses and 41 physicians at the nursing homes had given their written informed consent to participate in the trial. 105 filled in the evaluation form, of which nine were general practitioners. The educational intervention was appreciated by the participants. They considered that it was well worth the time, and appreciated both the content and form of the education and the facilitators for the intervention, Appendix VIII.

5 DISCUSSION

The studies included in this thesis have provided us with information on infections and treatment with antibiotics in outpatients (Paper I) and the elderly living in nursing homes (Paper II-IV and the pilot study). They have also contributed to the development of an educational intervention for the most common infections in elderly residents in nursing homes (Paper I-III and the pilot study). The intervention has been evaluated in terms of changes in antibiotic treatment, adherence to guidelines for lower UTI in women and appreciation by the participants (Paper IV). A summary of the main results:

- In the outpatient setting 59% of patients with infectious complaints were treated with antibiotics (Paper I). In nursing homes the corresponding figure was 84% (PaperII).
- Women with lower UTI were treated with a quinolone in 21% of the cases in the outpatient settings (Paper I) and in nursing homes 29% (Paper II).
- In 38% of the cases in nursing homes, the prescriptions of antibiotics were issued during an indirect contact with the physician i.e by phone, fax or e-mail.
- Half of the women with lower UTI in nursing homes, received a treatment which was not in line with the recommendations (Paper II).
- The focus group discussions (Paper III) have provided us with the perspective on the staffs' own experiences of infections in nursing homes. They have also increased our knowledge on barriers and facilitators to behavioural change within the process of antibiotic prescribing.
- The educational intervention had a modest effect on most outcome variables, including the primary outcome, but reduced the proportion of infections treated with an antibiotic by 12% (Paper IV).
- The participants of the intervention considered that it was well worth the time, and appreciated both the content and form of the education and the facilitators for the intervention (Appendix VIII).

5.1 RESULTS DISCUSSION

Pilot studies are seldom published, but they are important as they can improve the chances of success in the main trial [114]. The pilot study provided a feasible method for developing an educational intervention and evaluating the prescribing pattern of antibiotics in nursing homes for the elderly. No nursing homes dropped out during the two-year study period, and the education sessions were appreciated by the participating physicians and nurses. The study was undertaken at a reasonable cost and effort to the participants.

The outpatient study, Paper I, shows that the prescribing pattern is seemingly in good accordance with the recommendations, with a high use of PcV for RTI and PcV or isoxazolylpenicillins for SSTI. For lower UTI in women there was surprisingly high prescribing of quinolones.

The results from Paper I and II informed us about some of the differences between the outpatient setting and the nursing home setting, in treatment with antibiotics. A higher proportion being treated with antibiotics in the nursing homes was expected due to the

pattern of diagnoses. UTI, SSTI and pneumonia in outpatients, also had a high level of treatment with antibiotics (87%, 74% and 89% respectively). Moreover, there is another explanation for the differences - the inclusion criteria for the DPS in SANT - as we registered those with an infectious symptom that required a physicians' opinion. In the nursing home the nurse acts as a gate keeper before a contact with the physician is made, which means that simple infections managed by the nurses were not included in the results of Paper II.

It may be questionable that the physician was not present in the nursing homes when 38% of the antibiotics were prescribed, but as long as there is a nurse with competence and skills in dealing with the most common infections in the elderly, the physicians would often not be any wiser by physically visiting the nursing home resident if you consider for example the main diagnosis-lower UTI. However, it is important for the managers of the nursing homes to keep this in mind when they plan the nurses' professional development. In the More and Romsdal prescription study for outpatients in Norway, by Rokstad and Straand 1997, the corresponding figure was 25% [115].

The indications for antibiotic treatment are generally in accordance with other studies, both in outpatients, where RTI are the most common indication [116-118] and in nursing homes with UTI as the main indication for antibiotics [46, 47, 67, 119-120]. However a point-prevalence study in the county of Västra Götaland 2004 had SSTI as a more common indication for antibiotics, 36%, but as the authors pointed out this could be explained by long-term treatments for chronic ulcers which can lead to a higher proportion of patients on antibiotic treatment in a point-prevalence study compared to an incidence study [66]. The prescribing of quinolones for UTI was higher in our nursing homes, 34%, than in other studies in Sweden where it has ranged from 21% to 26% [46, 47, 66]. Bredmose-Hansen *et al.* 2002, presented the results in four different municipalities where the proportion of quinolones for UTI ranged from 15.4% to 42.6% [47]. The diagnosis-prescribing survey done in 2000 (Paper I) was repeated in 2002 and 2005. The results are quite similar between the years, but there has been a decline in antibiotic prescription for RTI, however no change for UTI and SSTI was noted. For lower UTI, the prescribing of pivmecillinam had increased while trimethoprim had decreased significantly between 2002 and 2005. There was no significant change in the prescribing of quinolones for lower UTI. The relative prescribing of nitrofurantoin had increased significantly from 2000 to 2002 and with a further, but not significant, increase in 2005 [30].

The focus group discussions (Paper III) made it clear that the nurses have a key role in the antibiotic prescribing process in the nursing homes, which is also supported in Walker *et al.* 2000 [121]. The shared experiences on infections, antibiotic treatment and possible barriers and facilitators for change provided by the participants in the focus group discussions, were very valuable in the planning of the intervention. The management of infections seems to be highly dependent on the characteristics of the people involved in the process. The focus group discussions also put words to the subtle symptoms interpreted as UTI in the elderly, that can trigger ordering of cultures and prescribing of antibiotics. Juthani-Metha *et al*. 2009, described the clinical presentations associated with positive urine culture, and found that dysuria, change in character of urine, and change in mental status were significantly associated with the

combined outcome of bacteriuria and pyuria. It also showed that almost two-thirds of the clinically suspected UTIs had a negative urine culture, which points out the risk of overdiagnosing UTI within this population [39]. The summary of what Walker *et al.* 2000 refer to as "issues and themes": Nurses' and physicians' interpretation of bacteriuria as "symptomatic" in the presence of nonspecific symptoms; the ordering of urine cultures for nonspecific changes in a resident's status, the central role of the nurse in communicating nonspecific changes in the health status of a resident to physicians and family members; the difficulty in eliciting information about symptoms from frail elderly residents; uncertainty of physicians about the significance and management of a positive urine culture result; concern over liability of nurses and physicians [121] reminds us in many ways about the categories that emerged from our focus group discussions: Symptoms of urinary tract infections - clinical signs and attitudes; What leads to antibiotic prescribing?; What does a positive dipstick or positive urine culture mean?; Communication between the staff concerning infectious symptoms; Hygiene in the nursing home setting. The results are quite similar despite the fact that narrower objectives were presented to the participants before the sessions that the discussions would be about ordering of urine cultures and the prescribing of antibiotics for asymptomatic bacteriuria. This could indicate that it is not important, perhaps not even advisable, to be too focused in focus group discussions when your aim is to explore something. If the subject is relevant to the participants, they will narrow it down themselves to what they think is the most significant part of the discussion. In that way you minimise the risk of contaminating the discussion with your own preconceptions.

In Paper IV, the statistically significant result of lowering the total prescribing of antibiotics was unexpected as Sweden is a low-prescribing country with respect to antibiotics [26]. Some would argue that lowering antibiotic prescribing with 12% is not a modest effect, especially if you could achieve a 12% sustainable decrease on a global basis. It is an average effect compared to other interventions targeting antibiotic treatment [97]. There was indeed an improvement of adherence to the guidelines during the post-intervention DPS, in comparison to the baseline DPS. The use of recommended antibiotics for lower UTI had increased and the prescribing of quinolones was lower after the intervention. However, these results could not be attributed to the intervention, as the change was similar in the control group. This could indicate that another intervention rather than ours had influenced the prescribing pattern of antibiotics. There is no specific intervention that we know of other than what is already mentioned in the paper i.e the active Strama work that seems to have had an impact on the prescribing behaviour in Sweden during the time of our study [122]. The reduction in UTI was lower in the intervention group than in the control group. We do not know the reasons for that, but it could be attributed to the lower antibiotic usage causing recurrence of infections. However, if that was the case, those infections should have been recorded as recurrent UTI in the form and we could not see any difference between the groups concerning recurrent UTI.

5.2 METHODOLOGICAL CONSIDERATIONS

For cross-sectional studies (Paper I and II) it is crucial to have a representative sample if generalisations of the results are to have any validity. In paper I there are some

problems that we can mention: The included prescriber categories only represents 70-75% of the prescriptions of antibiotics; the number of forms returned per 1000 inhabitants ranged from 3.73 to 7.68 for the 5 counties; and the actual response rate is difficult to assess. It could give a skew picture of the diagnosis and treatment pattern if the responses were elective in their nature e.g. if only those physicians that already comply with the guidelines are the ones responding or if they only include the patients when they know a prescription of antibiotics was justified. If the response rate is high, the problem with physicians randomly choosing not to respond in the survey would be a minor one. Today we have data from repeated similar surveys made in 2002 and 2005. Those surveys have not provided any unexpected results that give us reason to question the validity [30]. As the result from this study is also consistent with other similar studies it is fair to conclude that the sample was reasonably representative [116-118].

The cross-sectional study in Paper II also deals with some difficulties due to representativeness and response rate. The prescribing of antibiotics was a little bit lower than earlier studies [46, 47, 67] which could indicate that our sample of nursing homes has a greater interest within the area of infections and antibiotic prescribing and thus are already more compliant with guidelines than average nursing homes. The documentation of the forms was made by the nurses, which raises the issue of reporting bias. This was at first a balance between getting a high response rate and validity of the information provided in the forms. But looking at studies in other fields, such as reporting of adverse events - there could be advantages involving the nurses in reporting, both to increase reporting rates [123] but also in terms of increased validity [124]. The validity of the diagnoses could be questioned, as there was no clear definition, or a second opinion from a specialist within infectious diseases or a second opinion from a peer. However, our objective was not to study this under ideal conditions, but to get information about the real world scenario in the nursing homes.

The use of mixed methods in paper III added more strength to the results than if the focus group discussions alone had been presented. The results indicate that the use of different methods can yield different results. For example, if we should have settled for the KA-questionnaire, we would not have had anything indicating the importance of the nurses in the prescribing process of antibiotics, which can be illustrated with the quote from one of the GPs participating: “I believe that a nurse who wants the patient to get a treatment, achieves this by describing (the symptoms/health status) in a certain way. I am totally convinced. This is part of the interplay we have – nothing strange about that, really.”

The strength of focus group discussions (Paper III) is mainly in that it enables interaction between the participants [103, 125]. There are different orientations within this field of qualitative research, and Freeman 2006, means that the different and sometimes contradicting advice on ‘best practice’ when conducting focus group discussion, originates from the researcher’s epistemological perspective – realist or constructivist [102]. Mays and Pope 2000, also describes how relativists and subtle realists differ in their views on how to assess quality in qualitative research [126], which is also discussed in the review of Rolfe 2006 [127]. Choosing homogenic or heterogenic groups; pre-existing groups or not, mainly depends on the objective and the nature of the topic of the focus group discussion. Krueger 1993, supports homogenous

groups, although he states that it is important to vary group composition and use several sub-groups, as this makes analysis of group differences easier and increases the transferability of the results. He means that heterogeneity in the groups is contrary to the basic point of conducting focus groups i.e making people feel free to share their perceptions and thoughts [125]. Kitzinger 1994, believes that working with pre-existing groups captures "social contexts within which ideas are formed and decisions made" [128]. There is a rationale to choosing pre-existing groups for discussions on sensitive topics, to make the participants more comfortable sharing their thoughts. We chose homogenous groups, not to enable an analysis of the difference between the groups, but to increase the possibilities of the participants sharing their thoughts and experiences. The hierarchy between the groups in our study could have posed a problem if we had used heterogenic groups [125]. The focus groups in Walker *et al.* 2000, were also homogenous, but they did not include nursing assistants [121]. The nursing assistants' experiences were important in our study as we needed knowledge about the whole antibiotic prescribing process from the nursing assistant to the formally prescribing general practitioner. One might then ask why we did not involve the residents or relatives to these focus group sessions. It would certainly have added another perspective to these discussions. However, our main interest and objective was in the professionals' interplay and communication. Reflexivity means sensitivity to how the researcher's preconceptions and experiences and the research process have influenced the collected data [126]. In our focus groups my experience from working in nursing homes and my professional background as a pharmacist cannot be ignored, but two of the co-authors: one research nurse and one social anthropologist, have read the full transcripts and the research nurse also analysed the data. Some researchers use respondent validation or 'member checking' as they believe it increases the credibility, which is debated in the reviews by Mays and Pope 2000 and Rolfe 2006 [126, 127].

Paper IV. As we wanted to know whether the intervention was effective in the real world, we chose a pragmatic approach. Cluster randomised controlled trial for evaluating an educational intervention is the golden standard, but the pragmatic approach created some difficulties in the conduction and analysis of the trial which are described below.

The modest effect of the intervention could be explained by several factors: i) low exposure or wrong participants in the intervention ii) a low agreement with the guidelines used iii) factors other than the intervention affecting our results.

i) The evaluation showed a low participation by the physicians in the intervention, which could partly explain the modest effect of the intervention. But achieving this result without the physicians taking an active part in the intervention further provided us with information about the nurses' key role in antibiotic prescribing in the nursing home setting. There were two control homes taking part of the intervention as the staff at these control homes had heard from staff at the intervention homes that an education would take place. This also points out the risk of contamination by staff working in different nursing homes in the same municipality, which would dilute the intervention effect.

ii) The modest effect could also be due to a low agreement with the guidelines used, which is rather unlikely as both the control group and the intervention group increased their adherence to the guidelines concerning the selection of antibiotics after the intervention.

iii) Other factors that might have influenced our results are *secular trends* such as the decrease in prescriptions of quinolones per 1000 inhabitants and day by 14% from 2003 to 2005 [122]. This was probably a result from general efforts made by drug therapeutic committees and local Strama-groups to increase adherence to treatment guidelines. *Hawthorne effect* is the effect that people tend to perform better when they know that they are being observed. As the intervention homes received more attention as they received the intervention there is a risk that they would report better compliance with the guidelines simply because they knew what we were studying. Actual performance was not studied. Due to feasibility, the *time frame* between the data collection and the intervention was long and varied between the nursing homes, which could have had an impact on the results. Many things happen during one year in a nursing home. The residents are different; staff could be different which means that those exposed to the intervention might not even work in the nursing home during the follow-up period. This was taken into consideration in the planning stage of the trial, as one inclusion criterion was a self-assessed stable staff situation. This could however change over time. The baseline data collection and the post-intervention data collection were conducted at different times of the year which raises the issue of *seasonality*. However, examining antibiotic prescribing in this age group shows that seasonality does not apply in a meaningful way, especially not to urinary tract infections in this patient group.

Selection bias refers to systematic differences between comparison groups. Random allocation protects from selection bias. The level of randomisation is a trade off between the risk of contamination and the number of clusters available. A small number of clusters may lead to chance imbalances between the randomised groups on individual factors such as baseline performance or characteristics of the clusters, which may influence the observed intervention effect. Stratification before randomisation on important variables, in our study number of UTI/residents and geographical regions, was a measure taken to prevent selection bias. Selection bias is also used to describe systematic differences between those who have been selected to participate in a study and those who were not selected. The relatively low antibiotic prescribing in our trial of 1.0 prescription per resident and year, indicates a risk of selection bias towards inclusion of nursing homes with less consumption of antibiotics and possibly more compliant with the guidelines to start with. As the situation was the same in the intervention and the control group at baseline this would not be a problem for the internal validity of the evaluation of the intervention effect unless the dropouts deviated from the average nursing homes (see attrition bias below). However, it could still cause problems for the external validity, generalisability, of the results. For example, the readiness to change stage could be different between nursing homes with a high prescribing of antibiotics compared to nursing homes with a low prescribing. These nursing homes would then respond in different ways to the intervention depending on their readiness to change according to the Prochaska's stages of change model [77, 78].

46 of the about 2600 nursing homes in Sweden participated in the whole trial and the results should be generalisable at least to low-prescribing nursing homes.

An *intention to treat* analysis, ITT, is the golden standard for analysing clinical trials because it reduces the risk of overestimating the effect on an intervention [129]. An ITT analysis was performed with respect to allocation, but because full outcome data was not available for all randomised nursing homes, we had to do the analysis for the 46 nursing homes remaining at follow-up, which is referred to as an available case analysis. How the dropouts have affected the results needed to be estimated as this analysis threatened the internal validity of the results.

Attrition bias If those who drop out of a study systematically differs from those who remain, this attrition of the original sample poses a threat to both the internal and external validity in a study, which is usually referred to as attrition bias [130]. The 20% drop-out of nursing homes is potentially a problem, in particular the considerably higher drop-out in the control arm. An exploratory analysis showed that dropout nursing homes did not differ from those remaining in the trial based on the baseline outcomes, which indicates that attrition bias is unlikely to have affected our results.

Type I error describes the error made if you reject the null hypothesis when it is in fact true i.e you find a difference between the groups in your sample, which does not exist in the population from which your sample was drawn. The primary outcome - quinolone use for women with lower UTI - did not differ between the arms, so the question on how much of the observed effect in the secondary outcomes that is related to type I error, arises. In clinical trials, significance levels are sometimes set lower for secondary outcome to avoid mass significance. If you perform *k* different tests each with a nominal significance level of α then: α = P(Rejecting a given test | H_0 for this test is true). The overall significance of the test procedure is, however, given by α^* = P(Rejecting at least one test | all H_0 are true) and $\alpha^* = 1-(1-\alpha)^k$. The probability of rejecting at least one test is thus greater than of rejecting a specific test. A significance level of 0.05 is common and for reasons of interpretation and comparison with other similar trials, the significance level for the secondary outcomes was also set to 0.05 although this means that the results on the secondary outcomes should be interpreted cautiously.

ICC would have been high if management of patients within nursing homes was very consistent, but there was a wide variation in practice across nursing homes. An ICC of 0.03 for the primary outcome is quite low, but still it makes the 95% CI wider.

To follow trends and evaluate the sustainability of the effect of the intervention it would have been desirable to increase the frequency of measurements to at least three. The time and funding did not allow us to do this. This would also have required an increased effort from the participants and risk of a higher drop-out rate.

Both from our experience and based on the literature, it is advisable to conduct a cluster randomised control trial to evaluate a multifaceted educational intervention, but the decline in quinolone prescriptions over time, clearly shows that the wrong primary outcome was chosen.

The national efforts for containing antibiotic resistance and lower the levels of antibiotic prescribing are an ongoing struggle. The suggested long-term antibiotic goal from Strama and the Swedish Association of Local Authorities and Regions for the Swedish population, is 250 prescriptions per 1000 inhabitants and year [131]. The literature and this intervention study suggest that more drastic methods than educational interventions must be applied to reach this goal, such as legislative interventions or financial incentives for health care centers. However, variations between different counties in Sweden are high. In 2009 the prescribing rate ranged from 311 to 430 prescriptions per 1000 inhabitants and year, which indicates that it should be possible for at least the high prescribing metropolitan areas to decrease the antibiotics to much lower levels.

6 CLINICAL IMPLICATIONS

Outpatients with an infectious complaint in the year 2000, would in more than half of the cases have received an antibiotic. If you were a woman with lower UTI in 2000, you would in two out of five cases have received a quinolone. If you were an older woman in 2003 with lower UTI living in a nursing home you would in one out of two cases not be treated according to the recommendations. In the worst case scenario you would have been prescribed a quinolone for too long a period of time, by a GP you had not met, for a diagnosis you might not have had to begin with. Prescribing of antibiotics is a complex process and in nursing homes interpersonal relations between the staff and also the resident or relatives seem to be important determinants for the outcome.

In clinical practice the intervention effect would mean a reduction of approximately 6 prescriptions of antibiotics during one year in a nursing home with 50 residents or about 12 020 prescriptions during one year for all residents in the Swedish nursing homes.

7 CONCLUSIONS

In outpatients, the prescribing pattern in general seems to be in accordance with the recommendations although some potential deviations could be discerned.

The educational intervention influenced the prescribing as it reduced the proportion of prescribed courses of antibiotics and made the physicians handle a larger proportion of infections by ‘wait and see’. But as no intervention effect could be seen for the other outcomes including the primary outcome - proportion of quinolones prescribed for lower UTI in women - the intervention only had a modest effect.

SANT included 46, at baseline 58, of about 2600 nursing homes in Sweden (2%). Education on infections and their treatment in nursing homes is continuously needed. Training should preferably include both physicians and nurses as a high proportion of antibiotics are issued without a direct contact with the physician. It is however essential for future educational interventions to understand the role of the nurses and physicians and their interplay in more detail for a successful intervention with a sustainable effect.

8 EPILOGUE

The picture of antibiotic prescribing we have provided, is a picture with some problems. The most important of them was the high use of quinolones for lower UTI in women and the lack of evidence for choosing the right treatment regimen i.e the dose and the length of treatment for this patient group. When we came to the nursing homes, a picture of prescribing emerged where the physician, rarely present at the nursing homes, gets second hand information via reports from the nursing assistants and nurses. When should we treat and when not? Is there any evidence? Identifying the problems, creating the intervention, we found out that although we are country of low-prescribing in antibiotics, we could decrease the antibiotic use further and make the physicians more prone to 'wait-and-see'.

New guidelines for treatment of lower UTI in women were finally(!) developed during an expert meeting in 2006 at the medical products agency in Sweden. A number of the participants at that meeting have, in varied roles taken part in this project: Ingrid Brännström, Otto Cars, Sigvard Mölstad, Christer Norman and Nils Rodhe. So now it is time to conduct a new intervention study on compliance with the new guidelines, which should be easier as they are updated, evidence based guidelines.

In 2008 and 2009, the guidelines for lower RTI and SSTI were also updated.

I hope that the phrase "based on experience" will more often be combined with "based on evidence". I am proud to have provided some of it.

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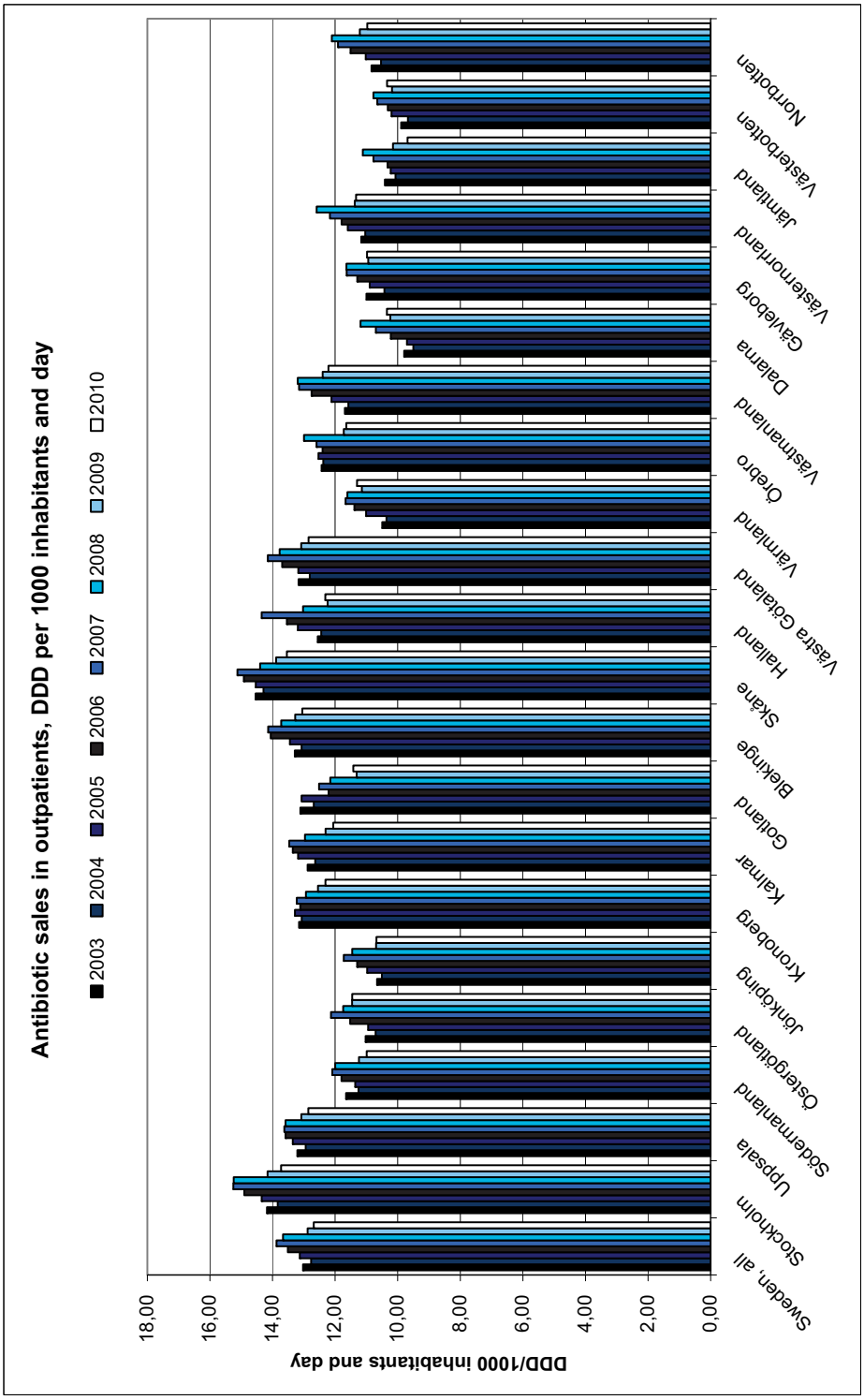
Appendix I


Antibiotic sales in outpatients, DDD per 1000 inhabitants and day
2003
2004
2005
2006
2007
2008
2009
2010
DDD/1000 inhabitants and day
18,00
16,00
14,00
12,00
10,00
8,00
6,00
4,00
2,00
0,00
Sweden, all
Stockholm
Uppsala
Södermanland
Östergötland
Jönköping
Kronoberg
Kalmar
Gotland
Blekinge
Skåne
Halland
Västra Götaland
Värmland
Örebro
Västmanland
Dalarna
Gävleborg
Västernorrland
Jämtland
Västerbotten
Norrbotten

Infections in nursing homes

One form per infection

1. **Date when GP was contacted** _____

2. **At what time was the GP contacted for this infection?**
☐ Daytime (workdays 8.00-17.00) ☐ other

3. **Kind of contact with GP?**
☐ Indirect contact (eg phone, e-mail, fax)
☐ Direct contact (GP was called in to the nursing home)
☐ Ordinary round

4. **GP's assessment**
☐ wait and see/advise ☐ diagnosis ☐ referral / hospitalization

5. **Resident**
Sex ☐ Man ☐ Woman Year of birth: ___ ___ Room N°/bed/apartm: ___

6. **Duration of symptoms in days**
☐ < 1 ☐ 1-3 ☐ 4-7 ☐ > 7

---

7. **Has the resident:**
a) had the same kind of infection during the last 3 months? **Yes** ☐ **No** ☐
b) been treated with antibiotics the last 3 months? **Yes** ☐ **No** ☐

8. **Treatment with antibiotics, methenamine hippurate or estrogen?**
☐ no ☐ already on treatment, no change
☐ Yes, with the following:

Name of the drug	Duration of treatment, in days

9. **Diagnostics:** **No** ☐ **Yes** ☐ **If yes, please select below**

U-leukocytes	☐ -	☐ +	☐ ++	☐ +++ or more	
U-nitrite	☐ negative		☐ positive		
U-sediment	☐ negative		☐ positive		
CRP	☐ < 10 mg/L	☐ 10-24	☐ 25-49	☐ 50-99	☐ > 100
WBC/ Leucocytes	☐ < 4	☐ 4-9	☐ 10-14	☐ > 14	
ESR	Yes ☐ Value: _____				

Temp _____°C urine culture ☐ other culture ☐
Other _____

10. **Does the resident have (you can mark more than one choice)**
☐ urinary catether ☐ incontinence protection ☐ estrogen
☐ Methenamine hippurate ☐ seasonal influenza immunisation

11. **Diagnosis (always mark ONE diagnosis, irrespective of treatment)**

Respiratory tract
☐ URTI
☐ pneumonia
☐ atypical pneumonia (eg mykoplasma)
☐ influenza
☐ Bronchitis, acute
☐ Bronchitis, exacerbation of chronic bronchitis/COPD
☐ caugh caused by an infection

Urinary tract
☐ lower UTI ☐ upper UTI
☐ recurrent UTI ☐ urethritis
(≥ 2 episodes within 6 months or ≥ 3 within 1 year)

Skin- and soft tissue
☐ erysipelas ☐ diabetic foot infection
☐ leg ulcer ☐ boil, abscess, wound infection, impetigo
☐ pressure ulcers

Other
☐ fever, uncertain cause
☐ unspecified virosis ☐ other diagnosis: ……

12. **Mark here if the choice of treatment e.g. the initiation of antibiotic treatment or choice of antibiotics, was affected by any of the factors below:**

☐ COPD ☐ Access to drugs
☐ Diabetes ☐ Urinary catheter
☐ Poor general health ☐ Several diagnoses possible
☐ Known hypersensitivity ☐ Therapy failure
☐ Other: _____

SEE THE INSTRUCTIONS

WHEN COMPLETED, PLEASE PUT THE FORM IN THE STUDY FILE

Nursing home: _____ Date:_____

A. General information

1. **Number of residents : _____ Men: ____ Women: ____**

2. **Number of rooms/apartments: _____**

3. **Average age: _____ Min/Max ____ years to ____ years**

B. Special needs

4. **How many of the residents can manage by themselves:**

	Hygiene	Clothing	Movement	Toilet	Eating
Number of residents					

C. Human resourses

5. **Man-labour year and time for GP's round each week**

Nurses	
Assistants	
Nurses' assistants	
Time for GP's round per week (hours)	

D. Health care indicators

6. **Deviation handling**

Number of deviations related to drugs	Number of Adverse Drug Reactions

7. **Falling accidents during the last year**

Number of falling accidents	Number of fractures

Appendix III

Nursing home: _____ Date:_____

8. How many of the residents…

are given injectable drugs on a regular basis? _____

have urinary catheter? _____

have leg ulcer? _____

have pressure ulcer? _____

9. Have you had any outbreak of vomiting/diarrhoea in the nursing home during the last year? Yes ☐ No ☐

10. Do you have a written routine for seasonal influenza immunization? Yes ☐ No ☐

11. Proportion of residents immunized against influenza (~%)? _____

12. Can you do dipslide culture (e.g. Uricult®) at the nursing home? Yes ☐ No ☐

13. Do you have written routines for diagnostic tests on suspicion of UTI? Yes ☐ No ☐

14. Do you have disinfection alcohol available at each:

Unit Yes ☐ No ☐

Floor Yes ☐ No ☐

Room Yes ☐ No ☐

15. How much disinfection alcohol has been used during the last month? _____ **Litre**

16. Do you have written routines about:

- **Use of disinfection alcohol** Yes ☐ No ☐
- **Use of disposable gloves** Yes ☐ No ☐
- **Use of protection work wear (disposable apron/robes)?** Yes ☐ No ☐

THANK YOU FOR YOUR PARTICIPATION!

PLEASE KEEP THE COMPLETED FORM IN YOUR STUDY FILE

Kunskaps/Attitydenkät för Urinvägsinfektioner vid särskilda boenden. Ifylld enkät sätts in i SANT-pärmen.

Datum: _____

Utbildning

Läkare o Leg år_____
Specialistkompetens o Nej
o Ja, i så fall ange inom vilket område _____

Anställningsform / anknytning till boendet

Tillsvidareanställning o
Stafettläkare o
Vikariat o
Tillfälligt inkallad o
Annat o _____

Hur länge har Du haft kontakt med detta särskilda boende?

_____ år

Nedan finner du flera påståenden kring UVI. Ange för varje påstående om Du anser att det är sant eller falskt eller om Du inte vet om det är sant eller falskt.

A. Symtombilden hos äldre

1. Förvirring kan vara det enda symtomet hos äldre med UVI

   Sant o Falskt o Vet inte o

2. Vid UVI som kräver antibiotikabehandling är feber alltid ett symtom

   Sant o Falskt o Vet inte o

B. Diagnostik

3. Om den boende har feber och symtom som tyder på UVI ska man göra en odling.
   Sant o Falskt o Vet inte o

4. Vid fynd av bakterier i urinen ska man alltid behandla.
   Sant o Falskt o Vet inte o

5. Falskt negativt nitrittest kan bero på följande:

   a. Kort blåsinkubationstid o Sant o Falskt o Vet inte
   b. Lågt bakterieantal i urinen o Sant o Falskt o Vet inte
   c. Intag av höga doser C-vitamin o Sant o Falskt o Vet inte
   d. Intag av järntabletter o Sant o Falskt o Vet inte
   e. Bakteriearten går ej att påvisa o Sant o Falskt o Vet inte

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

6. Falskt positivt nitrittest kan bero på följande:

a. Vissa läkemedel o Sant o Falskt o Vet inte
b. Fördröjd avläsningstid o Sant o Falskt o Vet inte

7. i) Urin till nitrittestet bör tas från: (Rangordna även följande alternativ där 1 är det som är bäst) ii) Rangordning

a. Blöja o Ja o Nej o Vet inte __
b. Kvällsurin o Ja o Nej o Vet inte __
c. Morgonurin o Ja o Nej o Vet inte __

ii) Urin från KAD, kvarkateter, ger tillförlitliga resultat på nitritstickan

Sant o Falskt o Vet inte o

C. Behandling, generellt

8. Om en patient får tillbaka en okomplicerad (nedre) UVI inom två månader efter första episoden, bör läkaren välja ett annat preparat än han/hon gjorde första gången pga risken för resistensutveckling.

Sant o Falskt o Vet inte o

9. Jag anser att antibiotikakurerna vid okomplicerad (nedre) UVI på särskilda boenden ofta är

a. För korta o
b. För långa o
c. Lagom långa o
d. Inget av ovanstående o

10. Jag anser att man ofta
a. Överbehandlar UVI hos äldre på särskilda boenden o
b. Underbehandlar UVI hos äldre på särskilda boenden o
e. Inget av ovanstående o

11.

a. När äldre män har UVI ska man vid behandlingsvalet alltid ta hänsyn till att prostata kan vara inblandad
Sant o Falskt o Vet inte o

b. Vid UVI ska man behandla äldre män med längre antibiotikakurer än äldre kvinnor
Sant o Falskt o Vet inte o

D. Fallbeskrivningar

12. Astrid, 82 år bor på boendet Storken. Hon har besvär som tyder på okomplicerad (nedre) UVI, vilket bekräftas av läkare. Astrid är allergisk mot penicillinpreparat.

a. Bactrim (trimetoprim-sulfa) är förstahandspreparat i detta fall
Sant o Falskt o Vet inte o

b. Furadantin (nitrofurantoin) är ett av de rekommenderade medlen
Sant o Falskt o Vet inte o

c. Cefamox (cefadroxil) är ett av de rekommenderade medlen
Sant o Falskt o Vet inte o

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

13. Elin, 76 år som också bor på Storken har haft smärtsamma och frekventa miktioner de senaste två dagarna. Nitrittestet som tas av sjuksköterskan på boendet är positivt.

a. Eftersom nitrittestet är positivt behöver inte sedimentet kontrolleras
Sant o Falskt o Vet inte o

b. Eftersom nitrittestet är positivt behöver ingen urinodling göras
Sant o Falskt o Vet inte o

c. Eftersom nitrittestet är positivt behöver ingen dipslide göras
Sant o Falskt o Vet inte o

Allmänläkaren drar slutsatsen att Elin har en okomplicerad (nedre) UVI och bestämmer sig för att behandla henne med Trimetoprim. Allmänläkaren vill få in ytterligare ett urinprov efter avslutad behandling som en behandlingskontroll.

d. Att kontrollera urinen efter behandlingen är korrekt i detta fall
Sant o Falskt o Vet inte o

14. Elin, 76 år (se fråga 13) får åter besvär med urinvägarna två månader senare. Läkaren sätter åter in antibiotika efter konstaterad okomplicerad (nedre) UVI.

a. Trimetoprim kan rekommenderas i detta fall
Sant o Falskt o Vet inte o

b. Selexid (pivmecillinam) kan rekommenderas i detta fall
Sant o Falskt o Vet inte o

c. Kinoloner exempelvis Lexinor (norfloxacin) är att rekommendera eftersom patienten fick trimetoprim förra gången
Sant o Falskt o Vet inte o

d. Trimetoprim + sulfa exempelvis Bactrim vore att föredra eftersom patienten endast fick trimetoprim förra gången
Sant o Falskt o Vet inte o

15. Elin (se 13-14) har ständiga problem med urinvägarna. Sjuksköterskan undrar vad hon ska göra. Läkaren föreslår att de ska prova lågpotent östrogen (östriol) i tablettform eftersom Elin har sköra slemhinnor.

a. Östriol kan ha en positiv effekt i detta fall
Sant o Falskt o Vet inte o

b. Hiprex (metenaminhippurat) hade kunnat vara ett alternativ till östrogen
Sant o Falskt o Vet inte o

16. Berta 79, som bor på ett särskilt boende har fått diagnosen okomplicerad (nedre) UVI. Allmänläkaren behandlar henne med Selexid (pivmecillinam) 200 mg 3 gånger dagligen i 5 dagar.

a. Behandlingstidens längd är korrekt
Sant o Falskt o Vet inte o

b. Trimetoprim är billigare (=sant). Därför hade det varit ett bättre alternativ i detta fall.
Sant o Falskt o Vet inte o

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

Forts. 16

Berta får återigen besvär efter en månad och läkaren konstaterar okomplicerad (nedre) UVI. Denna gång förskriver allmänläkaren Selexid (pivmecillinam) 200 mg 3 gånger dagligen i 10 dagar.

c. Det var korrekt att öka behandlingstidens längd
Sant o Falskt o Vet inte o

17. Konrad 91, som bor i egen lägenhet på servicehuset Delsbo, har konstaterad UVI. Läkaren förskriver därför Trimetoprim 160 mg 2 gånger dagligen i 14 dagar.

a. Trimetoprim är ett korrekt val
Sant o Falskt o Vet inte o

b. Trimetoprim + sulfa t.ex Bactrim är att föredra
Sant o Falskt o Vet inte o

c. Ett kinolonpreparat (t.ex. Lexinor) vore det bästa för Konrad
Sant o Falskt o Vet inte o

d. Behandlingstiden, 14 dagar, är för lång
Sant o Falskt o Vet inte o

18. Ernst 79, har UVI med misstanke om prostataengagemang.

c. Trimetoprim 160 mg 2 gånger dagligen i 14 dagar är ett bra alternativ
Sant o Falskt o Vet inte o

d. Lexinor (norfloxacin) är ett bättre alternativ än trimetoprim i detta fall
Sant o Falskt o Vet inte o

19. Ester 82, har inte mått bra de senaste två dagarna. Nitrittestet är positivt. Hon har ingen feber och har KAD (kvarkateter). Sjuksköterskan ringer och undrar om hon kan börja ge en antibiotikakur. Allmänläkaren tycker att det låter bra och föreslår att hon tar Selexid (pivmecillinam) som finns i läkemedelskåpet eftersom Ester fick Trimetoprim för två månader sedan.

a. Det är korrekt att ordinera antibiotika i detta fall
Sant o Falskt o Vet inte o

b. Byte av preparat rekommenderas trots att Trimetoprim fungerade bra förra gången
Sant o Falskt o Vet inte o

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

E. Nedan finner Du ett antal påståenden angående urinvägsinfektioner hos äldre på särskilda boenden. Ange om Du instämmer eller ej i dessa påståenden genom att markera den ruta som bäst överensstämmer med din åsikt.

20. En okomplicerad nedre UVI hos en kvinna över 65 år ska behandlas med antibiotika under minst 7 dagar

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

21. När en kvinna som bor på ett särskilt boende får upprepade okomplicerade UVI inom några månader ska ett annat antibiotika väljas än det som skrevs ut vid första episoden.

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

22. Till postmenopausala kvinnor med återkommande UVI kan ett peroralt lågdosöstrogenpreparat vara av värde.

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

23. Till postmenopausala kvinnor med återkommande UVI kan ett lokalt östrogenpreparat vara av värde.

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

24. Sjuksköterskan bestämmer i praktiken om urinvägsinfektioner ska behandlas eller inte

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

25. Sjuksköterskan bestämmer i praktiken vilket preparat som förskrivs vid urinvägsinfektioner

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

Ifylld enkät sätts in i SANT-pärmen

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

Kunskaps/Attitydenkät för Urinvägsinfektioner vid särskilda boenden. Ifylld enkät sätts in i SANT-pärmen.

Datum: _____

Utbildning

Sjuksköterska o Leg år ____
Vidareutbildning o Ja, i så fall ange inom vilket område _____
Distriktsköterska o

Anställningsform / anknytning till boendet

Tillsvidareanställning o
Pooltjänst o
Vikariat o
Tillfälligt inkallad o
Annat o _____

Hur länge har Du haft kontakt med detta särskilda boende?

_____ år

Nedan finner du flera påståenden kring UVI. Ange för varje påstående om Du anser att det är sant eller falskt eller om Du inte vet om det är sant eller falskt.

A. Symtombilden hos äldre

1. Förvirring kan vara det enda symtomet hos äldre med UVI

   Sant o Falskt o Vet inte o

2. Vid UVI som kräver antibiotikabehandling är feber alltid ett symtom

   Sant o Falskt o Vet inte o

B. Diagnostik

3. Om den boende har feber och symtom som tyder på UVI ska man göra en odling.
   Sant o Falskt o Vet inte o

4. Vid fynd av bakterier i urinen ska man alltid behandla.
   Sant o Falskt o Vet inte o

5. Falskt negativt nitrittest kan bero på följande:

   a. Kort blåsinkubationstid o Sant o Falskt o Vet inte
   b. Lågt bakterieantal i urinen o Sant o Falskt o Vet inte
   c. Intag av höga doser C-vitamin o Sant o Falskt o Vet inte
   d. Intag av järntabletter o Sant o Falskt o Vet inte
   e. Bakteriearten går ej att påvisa o Sant o Falskt o Vet inte

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

6. Falskt positivt nitrittest kan bero på följande:

a. Vissa läkemedel o Sant o Falskt o Vet inte
b. Fördröjd avläsningstid o Sant o Falskt o Vet inte

7.

i) Urin till nitrittestet tar jag från: (Rangordna även följande alternativ där 1 är det som är bäst)

				ii) Rangordning
a. Blöja	o Ja	o Nej	o Vet inte	__
b. Kvällsurin	o Ja	o Nej	o Vet inte	__
c. Morgonurin	o Ja	o Nej	o Vet inte	__

iii) Hur länge bör urinen minst ha stått i blåsan för att nitrittestet ska vara tillförlitligt?
o 15 min o 1 h o 4 h o 6 h

8. Urin från KAD, kvarkateter, ger tillförlitliga resultat på nitritstickan

Sant o Falskt o Vet inte o

9. Vem läser av stickor på ert boende?

Sjuksköterskor o Undersköterskor o Vårdbiträden o Det varierar o

C. Behandling, generellt

10. Om en patient får tillbaka en okomplicerad (nedre) UVI inom två månader efter första episoden, bör läkaren välja ett annat preparat än han/hon gjorde första gången pga risken för resistensutveckling.

Sant o Falskt o Vet inte o

11. Jag anser att antibiotikakurerna vid okomplicerad UVI på särskilda boenden ofta är

a. För korta o
b. För långa o
c. Lagom långa o
d. Inget av ovanstående o

12. Jag anser att man ofta
a. Överbehandlar UVI hos äldre på särskilda boenden o
b. Underbehandlar UVI hos äldre på särskilda boenden o
e. Inget av ovanstående o

D. Fallbeskrivningar

13. Elin, 76 år, bor på Storken har haft smärtsamma och frekventa miktioner de senaste två dagarna. Nitrittestet som tas av sjuksköterskan på boendet är positivt.

a. Eftersom nitrittestet är positivt behöver inte sedimentet kontrolleras
Sant o Falskt o Vet inte o

b. Eftersom nitrittestet är positivt behöver ingen urinodling göras
Sant o Falskt o Vet inte o

c. Eftersom nitrittestet är positivt behöver ingen dipslide göras

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

Sant o Falskt o Vet inte o

Forts. 13 Allmänläkaren drar slutsatsen att Elin har en okomplicerad (nedre) UVI och bestämmer sig för att behandla henne med Trimetoprim. Allmänläkaren vill få in ytterligare ett urinprov efter avslutad behandling som en behandlingskontroll.

d. Att kontrollera urinen efter behandlingen är korrekt i detta fall
Sant o Falskt o Vet inte o

14. Elin (se 13) har ständiga problem med urinvägarna. Sjuksköterskan undrar vad hon ska göra. Läkaren föreslår att de ska prova lågpotent östrogen (östriol) i tablettform eftersom Elin har sköra slemhinnor.

a. Östriol kan ha en positiv effekt i detta fall
Sant o Falskt o Vet inte o

b. Hiprex (metenaminhippurat) hade kunnat vara ett alternativ till östrogen
Sant o Falskt o Vet inte o

15. Berta 79, som bor på ett särskilt boende har fått diagnosen okomplicerad (nedre) UVI. Allmänläkaren behandlar henne med Selexid (pivmecillinam) 200 mg 3 gånger dagligen i 5 dagar.

a. Behandlingstidens längd är korrekt
Sant o Falskt o Vet inte o

Berta får återigen besvär efter en månad och läkaren konstaterar okomplicerad UVI. Denna gång förskriver allmänläkaren Selexid (pivmecillinam) 200 mg 3 gånger dagligen i 10 dagar.

b. Det var korrekt att öka behandlingstidens längd
Sant o Falskt o Vet inte o

16. Ernst 79, har konstaterad UVI.

a. När äldre män har UVI ska man vid behandlingsvalet alltid ta hänsyn till att prostata kan vara inblandad
Sant o Falskt o Vet inte o

b. Vid UVI ska man behandla äldre män med längre antibiotikakurer än äldre kvinnor
Sant o Falskt o Vet inte o

17. Ester 82, har inte mått bra de senaste två dagarna. Nitrittestet är positivt. Hon har ingen feber och har KAD (kvarkateter). Sjuksköterskan ringer och undrar om hon kan börja ge en antibiotikakur. Allmänläkaren tycker att det låter bra och föreslår att hon tar Selexid (pivmecillinam) som finns i läkemedelskåpet eftersom Ester fick Trimetoprim för två månader sedan.

a. Det är korrekt att ordinera antibiotika i detta fall
Sant o Falskt o Vet inte o

b. Byte av preparat rekommenderas trots att Trimetoprim fungerade bra förra gången
Sant o Falskt o Vet inte o

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

E. Nedan finner Du ett antal påståenden angående urinvägsinfektioner hos äldre på särskilda boenden. Ange om Du instämmer eller ej i dessa påståenden genom att markera den ruta som bäst överensstämmer med din åsikt.

18. En okomplicerad nedre UVI hos en kvinna över 65 år ska behandlas med antibiotika under minst 7 dagar

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

19. När en kvinna som bor på ett särskilt boende får upprepade okomplicerade UVI inom några månader ska ett annat antibiotika väljas än det som skrevs ut vid första episoden.

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

20. Till postmenopausala kvinnor med återkommande UVI kan ett peroralt lågdosöstrogenpreparat vara av värde.

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

21. Till postmenopausala kvinnor med återkommande UVI kan ett lokalt östrogenpreparat vara av värde.

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

22. Sjuksköterskan bestämmer i praktiken om urinvägsinfektioner ska behandlas eller inte

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

23. Sjuksköterskan bestämmer i praktiken vilket preparat som förskrivs vid urinvägsinfektioner

Instämmer inte alls	o	o	o	o	**Instämmer helt**
	1	**2**	**3**	**4**	

Ifylld enkät sätts in i SANT-pärmen

Okomplicerad (nedre) UVI = blåskatarr, akut cystit
Komplicerad (övre) UVI = njurbäckeninflammation, pyelonefrit

Appendix VI. Contribution of different parts in the thesis project in the development of the intervention

Potential part of the intervention	**Outpatient study**	**Pilot study**	**Focus groups**	**Baseline DPS**	**Baseline KA-questionnaire**	**Baseline NHQ**	**The Literature**	**Project group meetings**	**Actually adopted in the intervention**
UTI-focus	++	+++	+++	+++	NA	NA	+++	+	Yes
Including the nurses	NA	+	+++	NA	-	NA	+++	+	Yes
Treatment duration	NA	+++	+	+++	++	NA	+	+	Yes
Type of antibiotics	++	+++	+	+++	++	NA	+	+	Yes
ABU	NA	+++	++	NA	+	NA	+++	+	Yes
Hygiene	NA	+++	++	NA	+	++	+	++	Yes
Barriers to be addressed									
Knowledge	++	+++	+	+++	+	NA	+	+	Yes
Organisational	NA	+++	++	+	+	+	+	+	Discussed
Structural - location - building - protective measures hygiene	NA	+++	++	NA	NA	+++	+	+	Discussed
Social	NA	+++	++	NA	NA	NA	+	+	Discussed
Economical	NA	+++	+	NA	NA	NA	+	+	No
Attitudes	NA	+++	++	NA	+	NA	+	+	Discussed

+++ major influence of including it in the intervention
++ moderate influence of including it in the intervention
+ minor influence of including it in the intervention
- support exclusion from the intervention (contradicts)
NA – Not Applicable

SANT-trial, Swedish Antibiotic Nursing home Trial
A collaboration between Strama, Karolinska Institutet and Apoteket AB

We would like to have your views on the content and form of this continuing medical education. Mark to what extent you agree to the statements below. Put a circle around the figure you think have the best correlation to your own view.

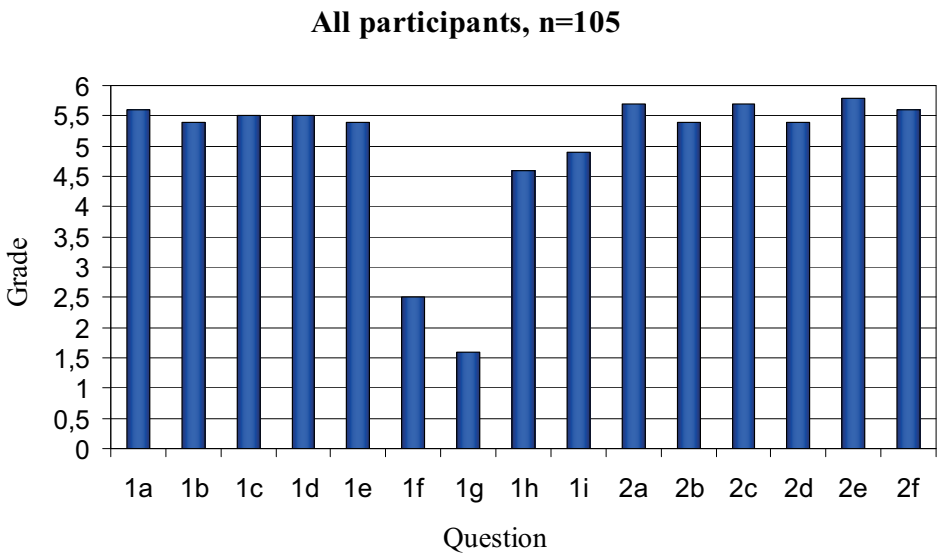
		Strongly disagree					Strongly agree
1.	a. The education was well worth the time	1	2	3	4	5	6
	b. I received good guidance for my everyday work	1	2	3	4	5	6
	c. The content of this meeting was worthwile for me	1	2	3	4	5	6
	d. The meeting was stimulating	1	2	3	4	5	6
	e. The meeting was well-structured	1	2	3	4	5	6
	f. I perceived as if I was dictated how to do my work	1	2	3	4	5	6
	g. To much time was spent on questions not related to the subject	1	2	3	4	5	6
	h. I think that the group regarded my knowledge and skills	1	2	3	4	5	6
	i. I think I regarded the knowledge and skills of the group	1	2	3	4	5	6
2.	a. The physician had adequate knowledge	1	2	3	4	5	6
	b. The physician stimulated the discussion	1	2	3	4	5	6
	c. The pharmacist had adequate knowledge	1	2	3	4	5	6
	d. The pharmacist stimulated the discussion	1	2	3	4	5	6
	e. The hygiene nurse had adequate knowledge	1	2	3	4	5	6
	f. The hygiene nurse stimulated the discussion	1	2	3	4	5	6

Profession (Nurse/physician):..... County: .....Date:.....

If you have any other views or suggestions you would like to share, please write on the reverse page. Thank You for your contribution!

Appendix VIII

Appendix VIII. Results from the participants' written evaluation of the educational intervention.



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Antibiotic Prescribing in Outpatients: a 1-Week Diagnosis–Prescribing Study in 5 Counties in Sweden

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A diagnosis–antibiotic prescribing study initiated by the Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance was performed in 5 counties in Sweden (total 1,290,000 inhabitants) during 1 week in November 2000. The aims of the study were to analyse diagnoses and antibiotics prescribed for outpatients and to appraise the feasibility of the data collection method. Physicians in primary care and departments of ENT, paediatrics and infectious diseases completed a questionnaire for each patient with an infectious disease complaint, including information about age, sex, diagnosis, diagnostic methods used and treatment. When an antibiotic was prescribed, the type and duration of treatment were noted. A total of 7,071 forms were returned, of which 7,029 included information on diagnosis; infections of the respiratory tract, urinary tract and the skin or soft tissues were responsible for 70%, 14% and 10% of the visits, respectively. Antibiotics were prescribed in 59% of all cases and phenoxymethylpenicillin was the most commonly prescribed antibiotic. Of the forms returned, 94% emanated from primary care centres. In conclusion, this study provides information on the treatment pattern associated with various diagnoses and the pattern of use of various antibiotics. Such a study is relatively simple to perform and entails only a small extra workload for the participants.

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INTRODUCTION

Antibiotic resistance is increasing worldwide and intensified measures are called for globally as well as in individual countries in order to curb this trend (1–3). There is a concern that the irrational use of antibiotics can contribute to this increase in resistance (1).

The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA) was initiated in 1994 as a national network in Sweden (4, 5) in order to give these issues national prominence. An increasing trend in the sale of antibiotics for systemic use was seen in Sweden at the end of the 1980s, from 14.1 defined daily doses (DDD)/1,000 inhabitants and days (TID) in 1986 to a peak in 1993 of 19.4 DDD/TID. Subsequently a decrease has occurred to a total of 15.8 DDD/TID in 1999 (6), of which 14.4 DDD/TID were dispensed for outpatients, a low figure from a European perspective, whereas a range between 8.9 and 36.5 DDD/TID was seen in 1997 (7).

In order to obtain detailed information concerning how various diseases are treated and for which diseases specific drugs are used, the Swedish Diagnosis Prescription Study (DPS) was initiated in 1978. Owing to a decreasing participation rate, in particular for general practitioners (GPs), its validity has been questioned and the study, in its present form, will be ended in 2002. It is important to create a valid and comparable picture of the proportion of patients with infectious symptoms who are prescribed antibiotics, for which diagnoses antibiotics are prescribed and the relations between different types of antibiotics for each diagnosis. Such information is essential in the development of both clinical practice guidelines and contextualized educational materials. The National Board of Health and Welfare in Sweden has proposed the development of a system (known as SPAR) for continuous follow-up of antibiotic prescribing and the reasons for prescribing, in hospitals as well as in outpatient care (8). However, the present study was conducted awaiting the implementation of this system. Recent statistics shows that $>90\%$ of antibiotics are prescribed for

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outpatients whereas ≈ 50% of both DDDs and prescriptions emanate from the primary care sector (6).

The main aim of this study was to present diagnosis and antibiotic-prescribing information for outpatients with infectious disease complaints in 5 counties in Sweden who sought treatment during a 1-week period. A further aim was to appraise the feasibility of this kind of survey and to see whether it could be recommended for possible use in the future.

MATERIALS AND METHODS

A prospective study was conducted simultaneously in 5 counties in Sweden during 1 week in November 2000. There are usually a high number of patients with infectious symptoms in November but winter epidemics of influenza and respiratory syncytial virus usually occur after this time. The participating counties were selected so as both to achieve a geographical spread and incorporate low-, medium and high-prescribing counties. The participating counties were Uppsala (16.5 DDD/TID), Östergötland (13.8 DDD/TID), Kronoberg (16.4 DDD/TID), Dalarna (12.9 DDD/TID) and Jämtland (12.7 DDD/TID), the figures in parentheses showing the sales of antibacterials for systemic use in 1999 (ATC code J01, version 1999; not including nitrofurantoin and fosfomycin) (6).

In each county, 1 or 2 persons were responsible for informing and communicating with participating doctors. These individuals were typically involved in local STRAMA groups working towards the rational use of antibiotics and were well known among their colleagues. In order to ensure anonymity, the participating doctors were usually recruited as part of teams in primary care centres or hospital departments. Both public and private surgeries, where available, were included. In total, 155 primary care centres (≈ 600 doctors), 24 hospital departments or specialized surgeries (ENT, infectious diseases and paediatrics) and 20 individual private practitioners agreed to participate. A number of measures were taken to ensure a high participation rate:

1. Written information regarding the study was in most cases provided twice to all potential participants;
2. Oral information was provided to key persons in each county; and
3. In some cases, information meetings were conducted for larger groups of doctors.

The study began at 08.00 on Monday 20 November, 2000 and ended at 08.00 on Monday 27 November, 2000. The physicians were asked to complete a form for all patients with a respiratory tract infection (RTI), a urinary tract infection (UTI), a skin/soft tissue infection or another type of infection. The forms were to be completed irrespective of whether the patient was prescribed an antibiotic or not. Only 1 diagnosis per form was to be given and only antibiotics for oral systemic use were included (ATC code J01, version 2001; includes nitrofurantoin and fosfomycin). Disorders normally treated with topical antibiotics, such as conjunctivitis, were excluded. The questionnaire form was a slightly modified version of 1 used previously in Finland (9, 10). The number of items was reduced in order to minimize the effort required from the participating doctors. The included items were discussed by members of the Swedish Study Group on Antibiotic Use following consultations with other practitioners. The final version of the form was piloted in a small group of GPs and found to be acceptable. The main topics of the questionnaire form are listed in Table I. For each item, the doctor was asked to choose between pre-formulated response alternatives but could use a written alternative when these were not considered suitable. The choice of antibiotic (generic or trade name) and the duration of treatment had to be written by hand. Dosage was not included. Detailed information for the doctor was printed on the reverse of each form. A full version of the questionnaire (in Swedish) is available from the corresponding author.

Table I. *Main topics included in the questionnaire*

1. Sex and year of birth
2. Visit: new, i.e. "first", visit or return visit. If return visit, was the patient already receiving antibiotic treatment?
3. Time of visit: working hours or emergency hours
4. Duration of symptoms (d)
5. Main diagnosis
6. Diagnostic techniques used
7. Treatment with antibiotics (yes/no), referral or both
8. Type of antibiotic and treatment duration
9. Factors influencing the choice of treatment

Each participating doctor collected the completed forms anonymously in envelopes. For each envelope, the county, physician category and type of surgery were recorded. The envelopes were sent to the Department of Public Health Sciences, Karolinska Institutet, Stockholm, where the data were entered into a computer and descriptively analysed using SPSS version 10.0. For this overall analysis it was decided not to separate the results into primary care and other outpatient care facilities, but to treat the data as a whole.

To validate the data, additional data were collected from Apoteket AB (National Corporation of Swedish Pharmacies). These data included data from each participating county concerning dispensed antibiotics for the week of the study, the week before and the week after. Furthermore, data were collected regarding the proportion of antibiotics prescribed by different physician categories in November 2000 from 2 counties (Dalarna and Uppsala). We calculated the number of completed forms per 1,000 inhabitants per county and the number of forms with prescribed antibiotic per dispensed antibiotic in each county during the study week. For all counties the percentage of forms emanating from primary care centres was calculated. In addition, for Uppsala and Dalarna, the proportion of dispensed antibiotic prescriptions emanating from primary care centres as a percentage of all the included types of department was analysed for the entire month of November 2000. These comparative data were analysed for face validity.

RESULTS

A total of 7,071 forms were returned and the forms were generally completed according to instructions. In a few cases (< 20), > 1 of the included diagnoses had been marked despite a clear instruction that only 1 diagnosis should be given. In those cases, by examining the diagnosis and the prescribed drug, the most relevant diagnosis was recorded. In some cases the form had also been completed for non-infectious symptoms or for drugs not belonging to ATC code J01. These forms were excluded from the analysis.

In the analysis, 7,029 patient cases were included. The remaining forms lacked diagnosis information. Of these 7,029 forms, 6,738 included information on the type of surgery, which in 92% of cases was primary care centres. There were 133 forms from ENT, 334 from paediatric and 100 from infectious disease departments. In 6,900 forms

both the sex (58% female, 42% male) and age of the patient was given. The age group for which the highest number of forms had been completed was children aged 0–7 y (25%; $n = 1718$) (Fig. 1).

In 84% of cases the visit was a first visit and 68% of the visits were made on weekdays between 08.00 and 17.00. The duration of symptoms before consultation was 1–7 d in 56% of cases but 17% of patients had had their symptoms for > 14 d.

A total of 70% of visits were for a RTI, 14% for a UTI, 10% for a skin/soft tissue infection and 6% for other infections. Overall, an antibiotic was prescribed in 59% of cases. The group of diagnoses with the highest rate of antibiotic prescriptions was UTIs (87%), followed by skin/soft tissue infections (74%) and RTIs (54%) (Table II). Detailed information on cases already receiving treatment and on referral/hospitalization is also presented per diagnosis.

On the form throat infections were divided into streptococcal tonsillitis and pharyngitis. In 779 cases the throat infection was classified as streptococcal tonsillitis. Of these, 98% were treated with an antibiotic. For the diagnosis pharyngitis, 10% were treated with antibiotics. Of the pneumonia cases $\approx 30\%$ were classified as atypical.

In 60% ($n = 4,248$) of cases with a given diagnosis some kind of diagnostic technique, as specified in the form, was used. The most common was the CRP test, which was used in 36% of RTIs, 15% of UTIs, 11% of skin/soft tissue infections and 42% of other infections. A diagnostic technique was used in 62% ($n = 2,586$) of the cases where an antibiotic was prescribed. The CRP test was also the most commonly used in this setting, being used in 44% of cases. For RTIs, a rapid streptococcal test was used in 27% of cases where an antibiotic was prescribed.

For RTIs, phenoxymethyl penicillin (PcV) was the most commonly prescribed antibiotic, being prescribed in 62% of cases, and tetracylines were the next commonest, being prescribed in 14% of cases (Table III). In UTIs, trimethoprim, extended-spectrum penicillins (almost exclusively pivmecillinam) and quinolones were prescribed in $\approx 30\%$ of cases each. Cotrimoxazole, fosfomycin and nitrofurantoin all had limited use. Of the skin/soft tissue infections treated with antibiotics, isoxazolyl penicillins (mainly flucloxacillin) were used in 51% of cases, PcV in 23% and cephalosporins in 12%.

The duration of treatment was provided in 4,082 cases. The overall duration of treatment varied from 1 to 360 d. For tonsillitis it was 10 d in 96% of cases. For uncomplicated UTI, a 7-day treatment duration was recommended in 77% of cases.

The choice of treatment was reported to be influenced by various specified factors (1 or more choices were possible) in 1,112 cases, the most common being that the patient was difficult to judge ($n = 340$). Therapeutic failure was mentioned in 194 cases, previous skin reactions or vomiting for penicillin in 97 cases, previous urticaria, etc. for penicillin in 83 cases, other diseases, such as diabetes, chronic obstructive pulmonary disease or other chronic diseases, in 292 cases and special requests by the patient in 188 cases.

The number of completed forms per 1,000 inhabitants ranged from 3.73 to 7.68 for the 5 counties, with a mean of 5.48. During the study week, a total of 9,820 prescriptions for oral antibiotics were dispensed in the 5 counties, with approximately the same numbers for the weeks before and after the study. The approximate proportion of antibiotics dispensed in the counties as revealed from the forms was 41% (range 33–48%). The physician specialities included in our study were responsible for $\approx 70\%$ of dispensed antibiotic prescriptions in Dalarna and Östergötland, where the prescriber category was examined for all prescriptions. When examining the primary care share of forms and dispensed prescriptions in those counties, the figures were almost identical at 93.3% and 93.5% for Dalarna and 91.1% and 91.0% for Östergötland, respectively.

DISCUSSION

This is the first large-scale study in Sweden to have collected information on physicians' treatments and choices of antibiotics for outpatients consulting for infectious symp-

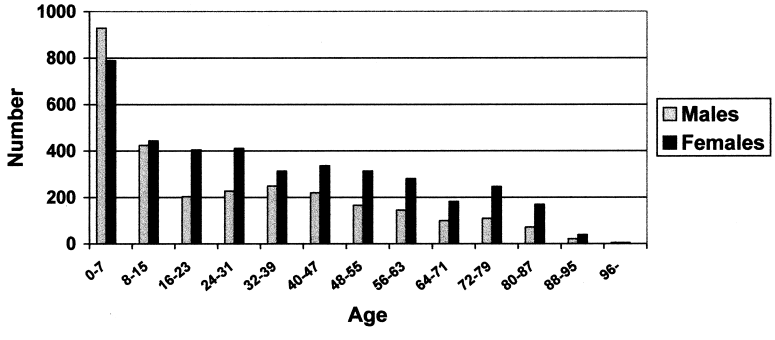

Fig. 1. The age and sex distributions of the included patients.

toms. The data make it possible to study the treatment patterns for various diagnoses as well as the patterns of use for various antibiotics.

The results confirm that RTIs are the most common infections encountered in outpatient care. They also show that Swedish physicians prescribe PcV to a high degree compared to physicians in other countries. In this study, PcV constituted 44% of all prescribed antibiotics, compared to a study in Norway in which the proportion was 32% (11) and studies in Finland in which the proportions were 17% (9) and 13% (10). The proportion of RTIs was almost the same in our study as in the Finnish studies, which were conducted in a similar way to ours. In the Norwegian study, the proportion of RTIs was somewhat lower.

For most diagnoses, the antibiotic prescribing pattern seemed to be in relatively good accordance with Swedish recommendations. PcV was prescribed in most cases of acute otitis media and acute pharyngotonsillitis, especially if cases of therapeutic failure or relapse were excluded. However, it was noted that $>90\%$ of children with acute otitis media were prescribed an antibiotic, despite the recently issued, and more restrictive, treatment recommendations for otitis media in children aged >2 y (12). Cases with the diagnosis pharyngitis were treated with antibiotics in only 10% of cases, compared to 21% in a Finnish study (9), which may reflect differences in treatment or diagnostic traditions. However, it is also possible that the high use of rapid streptococcal tests in this study influenced the pattern of diagnosis and that the diagnosis pharyngitis was used in this study when diagnostic tests were negative and the diagnosis tonsillitis when they were positive. According to Swedish tradition, isoxazolylpenicillins are often used for skin and soft tissue infections. This was also evident in this study, where $\approx 50\%$ of skin and soft tissue infections was treated with isoxazolylpenicillins whereas cephalosporins were only used in 12% of cases, as opposed to the situation in Finland where cephalosporins were used in 82% of cases (10). According to Swedish recommendations macrolides are not recommended as first-choice drugs in most situations and the dominance of erythromycin is probably due to therapeutic tradition, as other macrolides are also available.

Some potential deviations from guidelines could be discerned. It is, however, difficult to judge the appropriateness

Table II. *Diagnosis and cases with information regarding treatment*

		Cases with information on treatment ($n = 6{,}977$[a])		
Diagnosis	Total no. of cases ($n = 7{,}029$); *n* (%)	On treatment, no change ($n = 115$); *n*	Referral/ hospitalization ($n = 131$); *n*	Treatment with antibiotics ($n = 4{,}170$); % treated per diagnosis
Throat infection	1,193 (17)	10	7	70
URTI	1,276 (18)	11	5	7
Pneumonia	403 (6)	9	21	89
Influenza	20 (0.3)			10
Unspecified lower RTI	515 (7)	10	6	33
Otitis media	657 (9)	14	8	91
Sinusitis	393 (6)	10	1	94
Bronchitis, acute	411 (6)	9	2	50
Bronchitis, exacerbation of chronic bronchitis	75 (1)		1	87
RTI, all	4,943 (70)	73	54	54
Lower UTI	683 (10)	3		93
Recurrent UTI	136 (2)	3		89
Upper UTI	59 (0.8)	3	9	78
Urethritis	74 (1.1)	1		40
UTI, all	952 (14)	10	9	87
Erysipelas	83 (1.2)	2	7	82
Leg ulceration	52 (0.7)	6	2	67
Boil, abcess, ulcer, impetigo	369 (5)	9	7	78
Other	175 (2.5)	5	5	65
Skin/soft tissue infections, all	679 (10)	22	21	74
Other	455 (6)	10	50	32
All infections	7,029 (100)	115	131	59

[a] In total, 2,561 cases were given no treatment. The discrepancies in numbers are due to missing values.
URTI = upper respiratory tract infection; RTI = respiratory tract infection; UTI = urinary tract infection.

Table III. *Numbers of cases per antibiotic and per diagnosis*

Diagnosis	Penicillin V; J01CE02 ($n = 1,836$)	Amoxicillin, pivmecillinam, etc.; J01CA ($n = 422$)[a]	Flucloxacillin, etc. J01CF ($n = 268$)	Amoxicillin and clavulanic acid ($n = 74$)	Tetra-cyclines; J01A ($n = 461$)	Cephalosporins; J01DA ($n = 216$)[b]	Trimetho-prim; J01EA01 ($n = 274$)	Cotrimoxazole; J01EE01 ($n = 35$)	Macrolides; J01FA ($n = 286$[c])	Quinolones; J01MA ($n = 265$)	Other[d] ($n = 73$)	Total number of antibiotics per type of infection ($n = 4,173$[e])
Throat infection	700	10	–	3	2	71	–	2	27	–	11	832
URTI	48	8	–	2	15	2	–		18	–		93
Pneumonia	113	15	–	6	108	11	–	3	103	–	–	359
Influenza	1	–	–	–	1	–	–	–	–	–	–	2
Unspecified lower RTI	69	14	–	3	43	6	–	–	32	–	–	170
Otitis media	439	63	–	46	–	22	1	9	19	–	–	599
Sinusitis	228	34	–	9	75	8		1	21	–	1	377
Acute bronchitis	67	23	–	2	85	2	–	2		2	–	183
Exacerbation of chronic bronchitis	3	8	–		48	4	–	–	1	1	–	66
RTI, all	1,668	175	0	72	379	126	1	20	225	3	12	2,681
Lower UTI	–	198	1	–	5	16	236	4	1	149	27	637
Recurrent UTI	1	36	–	–	–	5	35	3	–	38	3	121
Upper UTI	–	1	–	–	–	1	1	6	–	37	–	46
Urethritis	1	1	1	–	19	–	–	–	1	9	1	33
UTI, all	2	236	2	0	24	22	272	13	2	233	31	837
Erysipelas	31	1	25	–	–	6	–	–	–	–	7	70
Leg ulceration, infected	2	–	27	–	1	3	–	–	–	3	2	38
Boil, abcess, ulcer, impetigo	51	6	164	–	1	33	–	1	11	5	18	290
Other skin infections	32	1	46	–	13	18	–	–	2	2	1	115
Skin/soft tissue infections, all	116	8	262	0	15	60	0	1	13	10	28	513
Other infections	50	4	4	2	43	8	1	1	8	19	2	142

[a] J01CA01, ampicillin 11, J01CA02, pivampicillin 1, J01CA04, amoxicillin 177, and J01CA08, pivmecillinam 233.
[b] 167 are for J01DA09 lorakarbef.
[c] 229 are for J01FA01 erythromycin.
[d] Clindamycin, 38 (11 tonsillitis, 1 sinusitis, 7 erysipelas, 2 infected leg ulcer, 16 boil, abscess, ulcer and impetigo, 1 other), fusidinic acid, 3 (2 impetigo, 1 other skin infections), phosphomycin, 7 (cystitis), nitrofurantoin, 24 (20 cystitis, 3 recurrent UTI, 1 urethritis) and vancomycin 1 (other infection).
[e] Differences compared to Table II are due to missing values and 17 cases of prescribing of 2 different antibiotics for the same patient.
URTI = upper respiratory tract infection; RTI = respiratory tract infection; UTI = urinary tract infection.

of prescribing in individual cases without a detailed examination of patient records or at the very least an analysis of the diagnostics measures taken.

A total of 33% of cases classified as unspecified lower RTI, which includes cough, were treated with an antibiotic, as well as 50% of cases of acute bronchitis. In addition, there was a relatively high proportion of tetracyclines prescribed for those infections, as well as for pneumonia and exacerbation of chronic bronchitis (Table III). It is, however, difficult to devise guidelines for unspecific diagnoses. The proportion of cases of acute bronchitis that were treated with an antibiotic was however lower compared to 1 of the Finnish studies (10), in which 71% of cases were treated.

The surprisingly high number of diagnostic tests made for RTIs, especially of CRP, requires further analysis.

Another example of a potential deviation from guidelines was that quinolones were used in 21% of females with a lower UTI, a non-recommended treatment (13). This level of non-recommended use was lower than figures reported in the DPS for 2000 (6) and in an earlier study (14). This may reflect a shift towards recommended drugs or may be because the DPS does not distinguish between complicated and uncomplicated UTIs. It may also be a sign of socially desirable responses.

To estimate the face validity of the data we made a number of comparisons, from which we drew the conclusion that the data could be regarded as a relatively good estimate of antibiotic prescribing in these counties during the study week. The inter-county variation in the number of forms returned per 1,000 inhabitants was 2-fold. This may depend on differences in physician availability but calls for a somewhat cautious interpretation of the data. When the number of forms with an antibiotic prescribed was divided by the total number of antibiotic prescriptions dispensed during the study week, the figures varied to a smaller degree. Finally, for the 2 counties where we compared the proportion of forms emanating from primary care centres during the study week to the proportion of dispensed prescriptions for the entire month of November in the same 2 counties emanating from primary care centres, the figures were amazingly similar. This is likely to indicate a more or less random inclusion of cases, and that the forms seem to correspond relatively well to reality for the included prescriber categories.

The actual response rate for the included prescriber categories is difficult to establish. Unpublished statistics from the county of Östergötland have previously shown that 43% of all antibiotic prescribing emanates from primary care centres. This corresponds well to our data. Theoretically, there are 2 main categories of low response rate:

1. Elected responses, where only physicians already complying with recommendations participate, or each participating physician fills in the forms only for some of his/her patients, those for whom the physician feels that the treatment was really justified, or shifting of diagnosis to a more "justified" diagnosis (15); and
2. Random responses, where the physician either participates or not and when s/he participates s/he fills in the form for most of the patients, without further analysis.

The consequences of these different response problems are somewhat different. In this study, the participating physicians remained anonymous, which should reduce the problems of elected responses, but such an influence could not be completely disregarded. Random responses are less problematic as long as the response rate is relatively high.

As the included prescriber categories only represent $\approx$ 70–75% of all prescriptions during the month when the study was done, it would be useful to include all prescriber categories for humans in future studies. It might be the case that the prescriber categories included here, due to extensive experience of antibiotic prescribing, have patterns that coincide relatively well with recommendations and that other prescriber categories less exposed to discussions regarding antibiotic use and resistance patterns might present a different prescribing pattern.

In conclusion, the method used in this study is simple and entails only a small extra workload for participants. It was found feasible to perform this type of study for a 1-week period. The results gave more detailed information regarding individual diagnosis compared to the regular DPS. Also, additional information, such as duration of symptoms before consultation and use of diagnostic techniques, was acquired for further analysis. The intention is to repeat the study using the same questionnaire form, for example every other year, in order to closely follow changes in diagnostic and treatment patterns for outpatients in Sweden.

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ORIGINAL ARTICLE

Infections and antibiotic prescribing in Swedish nursing homes: A cross-sectional study

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Abstract

The aim of this study was to present and assess the treatment of infections in Swedish nursing homes. It included 58 nursing homes with 3002 residents. During 3 months, nurses in the nursing homes recorded all infections requiring a physician's opinion. Of the 889 infectious episodes, 84% were treated with antibiotics. Many of the antibiotics were issued after indirect contact with the physician (38%). Indications for antibiotics were in 55% of the cases urinary tract infections (UTI), in 17% skin and soft-tissue infections and in 15% respiratory tract infections (RTI). The most common antibiotics were penicillins (38%), followed by quinolones (23%) and trimethoprim (18%). For the major indication, lower UTI in women, half of the cases were not treated according to the recommendations. The main concerns were length of treatment and overprescribing of quinolones. For the second major diagnosis, pneumonia, the high use of doxycycline could be questioned. Continuing education on infections and their treatment in nursing homes is needed. Training should preferably include both physicians and nurses as a high proportion of antibiotics is issued without direct contact with the physician.

Introduction

Antibiotics use is a major risk factor for development and spread of resistance, and increasing antibacterial resistance is a worldwide threat to public health [1]. Although Scandinavian countries have relatively low resistance rates, early actions are necessary as it seems difficult to reverse resistance once it has occurred [2].

In nursing home residents an association between resistance and higher mortality has been found [3]. In addition, a recently published study from Norway showed large variations in antibiotic sales to different nursing homes [4]. The management of infections in the elderly presents some particular difficulties related to clinical presentation, diagnostic testing and therapy [5–7]. Diagnostic uncertainty and treatment of asymptomatic bacteriuria (ABU) are examples of factors that might potentially contribute to antibiotic overuse [6,8,9].

In Sweden a general decline in total antibiotic sales had been observed since 1993 but, simultaneously, antibiotic sales had increased for patients 80 y of age and above [10]. Before this study little information was available on the indications for antibiotic treatment of infections in the elderly, in particular in terms of the elderly living in nursing homes. There were only a few regional studies available [11,12].

The Swedish Antibiotic Nursing Home Trial (SANT) is a collaborative project between Karolinska Institute, STRAMA (The Swedish Strategic Programme for the Rational use of Antimicrobial Agents) [13] and Apoteket AB (The National Corporation of Swedish Pharmacies). SANT was primarily started for 3 reasons: increasing antibiotic consumption in the elderly, a lack of knowledge about indications for treatment, and a lack of national studies in the area.

The aim of this paper is to present the prescribing of antibiotics and the indications for antibiotic treatment in the elderly residing in nursing homes. A secondary aim is to assess the antibiotic treatment

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in relation to the recommendations for the major indications.

Material and methods

This was a cross-sectional study. All registered nurses charged with the medical responsibility for nursing homes in Sweden were invited ($n = 366$) to participate in the study. Those who took an interest in the study forwarded the information to the nurses at the nursing homes in their area, who then decided to participate or not. Specialized nursing homes or wards (e.g. oncology wards) were excluded.

Questionnaires and data collection

Data collection was practically handled by the nurses at the nursing homes. A nursing home questionnaire was used to collect background data. The following variables were used: number of residents, gender distribution of the residents and the approximate proportion of residents that was expected to receive immunization against influenza

Nurses in Sweden are generally not allowed to prescribe antibiotics, so the nurses were asked to complete a form for all patients with infectious symptoms requiring a physician's opinion. Data were collected during 3 months, from mid-September to mid-December 2003. Recorded variables included patient data, when and how the physician was contacted, duration of symptoms before assessment by a physician, a number of preset diagnoses (as specified in Table I), diagnostic tests used, prescribed antibiotic, treatment length, use of urinary catheter and factors influencing the choice of treatment.

There was also a question on whether the resident had had the same kind of infection in the preceding 3 months, or had received any antibiotics during the preceding 3 months prior to recording. Recurrent UTI was defined as ≥ 2 episodes within 6 months or ≥ 3 episodes within 1 y (written on the form). The form was a modified version of one previously used in a diagnosis-prescription survey for outpatients in 5 Swedish counties [14].

The coordinator contacted all the study homes by telephone once before, once during and once at the end of the collection of diagnosis and prescribing data, reminding the participants of important dates and the proceedings of the trial. All the questionnaires and forms were pre-tested for face validity during a full-scale pilot study involving 7 nursing

Table I. Recorded diagnosis, proportion treated with antibiotics and number and type of diagnostics used per diagnosis during 3 months recording of infectious episodes in 58 nursing homes with 3002 residents in Sweden.

Diagnosis	Frequency; *n* (% of total)	Antibiotics; *n* (% of total)	Diagnostics were used[a]	Uristix	CRP	Culture	Other diagnostics[b]
URTI	18 (2.0)	10 (1.3)	9	1	6	–	2
Pneumonia	78 (8.8)	76 (9.9)	44	4	34	3	14
Atypical pneumonia	1 (0.1)	1 (0.1)	1	–	1	–	–
Influenza	1 (0.1)	1 (0.1)	–	–	–	–	–
Bronchitis, acute	12 (1.3)	11 (1.4)	6	–	5	–	1
Bronchitis, exacerbation of chronic bronchitis	11 (1.2)	11 (1.4)	4	–	2	–	3
Other, RTI	4 (0.4)	4 (0.5)	1	1	–	–	1
RTI, all	125 (14.1)	114 (14.8)	65	6	48	3	21
Lower UTI	317 (35.7)	270 (35.1)	298	252	23	147	56
Recurrent UTI	149 (16.8)	131 (17.0)	134	105	9	89	22
Upper UTI	21 (2.4)	18 (2.3)	19	17	5	7	7
Urethritis	2 (0.2)	1 (0.1)	1	1	–	1	–
UTI, all	489 (55.0)	420 (54.6)	452	375	37	244	85
Erysipelas	40 (4.5)	38 (4.9)	14	1	10	2	4
Leg ulcers	28 (3.1)	27 (3.5)	18	1	1	18	–
Pressure ulcers	12 (1.3)	11 (1.4)	7	–	2	5	1
Diabetic foot infection	4 (0.4)	4 (0.5)	2	–	–	2	–
Other, skin	60 (6.7)	48 (6.2)	18	–	3	14	1
Skin/soft tissue infections, all	144 (16.2)	128 (16.6)	59	2	16	41	6
Fever of unknown origin	13 (1.5)	7 (0.9)	1	2	7	3	3
Virosis of unknown origin	3 (0.3)	3 (0.4)	1	–	–	–	2
Other infections	62 (7.0)	62 (8.1)	17	31	23	27	18
Missing diagnoses	53 (6.0)	35 (4.6)	16	10	6	9	1
Total (n = 889)	889 (100)	769 (100)	611	426	137	327	136

[a]Any discrepancies between this column and the sum of diagnostics are due to multiple diagnostic methods for the different diagnoses.
[b]Dipslide culture, u-sediment, white cell blood count, X-ray, sedimentation rate, and diagnostics used ≤ 3 times.

homes. Some minor changes were made before the main study.

Analysis and statistics

The questionnaires were sent to the coordinator for entering and analysis of data using SPSS 10.0 software. The analysis of data mainly included proportion of antibiotics used for different diagnoses. For the major antibiotic indications, in particular lower UTI in women, the choice of antibiotics and duration of treatment was assessed in relation to the recommendations. For precision of the measurements, the 95% confidence interval is presented. The standard errors used for calculating confidence intervals are adjusted for clustering of antibiotic prescribing over nursing homes. The intracluster correlation coefficient, ICC, was 0.01. The data from the pilot study were not included in the analysis for this paper.

Ethics

The study was approved by the regional ethics committee in Stockholm. Written informed consent was obtained from participating nurses, physicians and unit directors at the nursing homes.

Results

65 nursing home located in 37 municipalities in 15 out of 24 counties were eligible for participation at the start of the study. Six nursing homes dropped out during the data collection process due to insufficient staffing, and 1 due to miscommunication.

The remaining 58 nursing homes had 3002 residents, of which 71% were women, with a mean age of 84 y. The average nursing home had 52 residents (median 40, range 14–207). According to estimations by the contact nurses, approximately 71% of the residents would receive immunization against influenza during 2003.

A total of 889 infectious episodes were recorded during the 3 months of data collection among the 3002 residents. The mean age of the residents with an infection was 85 y. Of all recorded episodes, 84% were treated with 1 or more antibiotic (excluding methenamine hippurate).

The antibiotic rate was 1.0 treatment per resident and y. In 38% of the cases, the prescriptions for antibiotics were issued during an indirect contact with the doctor, i.e. by phone, fax or e-mail. A specimen for culture was taken in 35% of the cases where a new prescription of antibiotics was issued.

A probable diagnosis was noted in 82% of the cases. Few cases were handled by 'wait-and-see' or referral (9% and 4%, respectively). It was common for the patients to have had the same kind of infection during the preceding 3 months (36%) and/or to have been treated with antibiotics during the preceding 3 months (43%). Diagnosis and diagnostics are presented in Table I. The distribution of antibiotics for RTI, UTI, skin and soft-tissue infections and other infections is presented in Table II.

The most common indications for antibiotics were UTIs (Table II). Men and women had the same rate of UTI (0.69 episodes per elderly and y). Diagnostics were used in most episodes (Table I). In 49% of the cases, a urine sample was taken for culture before issuing new antibiotics for UTI. The most common antibiotics prescribed for UTI were quinolones (34%).

It was noted that 88% (95% CI 0.79–0.97) of the quinolones prescribed to elderly women with a UTI ($n=85$) were used for lower or recurrent UTI. Of the 489 episodes of UTI, 212 had received antibiotics during the preceding 3 months and 211 had had the same kind of infection during the preceding 3 months.

For the major diagnosis, lower UTI in women ($n=226$), approximately half – 54% (95% CI 0.46–0.62) of the cases were not treated according to the recommendations. Either first-line antibiotics were not chosen (29%, 95% CI 0.21–0.36) and/or the treatment length deviated from the guidelines (47%, 95% CI 0.39–0.55). Of the 106 women with a non-recommended treatment length, 101 were treated too long. However, it is important to stress that men with lower UTI and incorrect treatment length in general received too short a treatment (39/40). The main antibiotics for lower UTI in women were pivmecillinam (32%), trimethoprim (30%) and quinolones (29%). Nitrofurantoin was only used in 8 cases. The treatment length was usually 7 or 10 d (56% and 13%, respectively). Treatment for 5 d or less only occurred in 9% of the treatments.

For skin and soft-tissue infections, a specimen for culture was taken in 24% of the cases before issuing a new antibiotic. Isoxazolylpenicillins were most commonly used (Table II). The duration of treatment was mainly 10 d (61%) and long-term treatment was rare (5%). Local treatment with fucidic acid represented only 1% of the treatments for skin and soft-tissue infections. Only 1 case was treated with a macrolide.

Among RTIs, the major diagnosis was pneumonia (Table I). A concomitant chronic obstructive pulmonary disease or multiple diagnoses possible was noted for 5 of these cases. Almost all cases of pneumonia were treated with antibiotics, most often with a tetracycline (33%) followed by penicillin V (25%) and amoxicillin (20%). In 34 cases, a CRP

Table II. Number of antibiotics prescribed for infections recorded during 3 months in 58 nursing homes with 3002 residents in Sweden[a].

Diagnosis	Frequency; n (%)	Penicillin V J01CE02	Other RTI penicillins J01C[b]	Tetra-cyclines J01A	Cephalo-sporins J01D	Quino-lones J01M	Trimetho-prim J01EA01	Piv-mecillinam J01CA08	Nitrofur-antoin J01XE01	Sulfa-trimethoprim J01EE01	Isoxazolyl-penicillins J01CF	Other	Antibiotics Total (%)
RTI	125 (14)	24	22	46	11	5	–	–	–	1	3	2	114 (15)
UTI	489 (55)	1	7	–	8	141	122	109	22	8	2	–	420 (55)
Skin/soft-tissue infection	144 (16)	17	1	–	11	8	1	1	–	–	73	16	128 (17)
Other infections[c]	78 (8)	6	6	3	6	12	4	2	–	4	8	21	72 (9)
Missing diagnosis	53 (6)	3	1	2	–	13	10	3	1	–	1	1	35 (5)
Total	889 (100)	51	37	51	36	179	137	115	23	13	87	40	769 (100)

[a]excluding methenamine hippurate (13 items).
[b]J01C, excluding J01CE02, J01CA08, J01CF.
[c]fever of unknown origin, virosis of unknown origin, eye infections and rare specific diagnosis.
RTI: respiratory tract infection; UTI: urinary tract infection.

was obtained and it was above 50 in 24 of these cases (Table I). The pneumonia cases were significantly older than other cases with a mean difference of 2 y (95% CI 0.1–4.4). Pneumonia was more common in men than in women (0.21, 95% CI 0.17–0.24), pneumonias per residing male and y compared to 0.07 (95% CI 0.05–0.10) among women. The most common duration of treatment was 10 d (48/63 cases).

Discussion

This is the first study on infectious episodes, which includes nursing homes, from a wide variety of locations in Sweden. A UTI was the most common indication for antibiotics and a quinolone was then most often the drug of choice. A large proportion of prescriptions of antibiotics was issued by the physician through an indirect contact with the nurse.

The antibiotic prescription rate found in this study (1.0 per resident and y) was a little lower compared to results published earlier where it has varied between 1.1 and 1.9 treatments per resident and y [11,12,15].

The proportion of antibiotics that was issued after an indirect contact with the physician, 38%, exceeded the figure found for outpatients in general in the More and Romsdal prescription study by Rokstad and Straand, 1997 (25%) [16]. This could be a potential risk for irrational prescribing of antibiotics, which in the long run could have negative effects on the resistance pattern for common pathogens in the nursing home setting.

In 2003, the recommended antibiotics for lower UTI in women, in Sweden, were pivmecillinam, nitrofurantoin or a cephalosporin for 5–7 d, or trimethoprim for 3–5 d. Approximately half of the cases of lower UTI in women were not treated according to these recommendations. Quinolones are only recommended for upper UTI and complicated UTI (including men). In this study, the use of quinolones was more frequent than in earlier studies in Sweden [11,12,17]. In studies from Norway on antibiotics in nursing homes, nitrofurantoin has been used to a much higher extent, whereas the use of quinolones has been small [4,15].

Asymptomatic bacteriuria is known to be very common in nursing homes, in particular in elderly women, which might lead to diagnostic problems, especially in patients with decreased cognitive function [8,9]. Our data do not allow an evaluation of the diagnostic procedure or the outcome of treatment, but it would be important to discuss with staff how diagnostics are used and interpreted. Even though most UTI was diagnosed in women, the UTI rate was equal for men and women.

Pneumonia was common, equivalent to 113 episodes per 1000 nursing home residents and y. The choice of antibiotics could be discussed. Doxycycline is not a first-line drug for pneumonia in Sweden. Considering the aetiology, penicillin V should be the most prescribed antibiotic followed by amoxicillin [18]. A concomitant chronic obstructive pulmonary disease could justify the choice of doxycycline but this was only noted for a few cases. Although the reasons for the high doxycycline use is beyond the scope of this paper, doxycycline might have been preferred because of practical advantages such as a small tablet taken once daily or a wish to cover more uncommon agents.

The use of antibiotics for skin and soft-tissue infections were mainly in line with current recommendations. Isoxazolylpenicillins dominated the prescribing pattern and the use of cephalosporins and macrolides was found to be low. Locally administered antibiotics and long-term treatment with antibiotics for skin and soft-tissue infections was not common.

The antibiotic prescribing for infections in nursing homes shown in this study, especially the high use of quinolones, could be a potential risk for the spread of resistant bacteria [19]. Spread of resistant clones has been shown to occur within nursing homes as well as between different health care facilities [19–21]. However, since the aim of this study was not to assess the ecological situation in nursing homes, we did not collect data on resistance.

Few nursing homes dropped out during the data collection. As the study included a large number of nursing homes of different sizes, from both rural and urban locations, the results can give an indication of the general situation in Swedish nursing homes. In this study only the infectious episodes, where the nurses considered a physician's opinion necessary, were recorded. This may lead to differences in the number of registrations and type of contact depending on the knowledge of the nurse or the availability of the physician at the different nursing homes. The extent to which we may have missed cases cannot be assessed. Such cases are more likely to have gone untreated, so the overall effect on the results would probably be an overestimation of antibiotic treatment. The limitations of this study are mainly associated with 1) the validity of the diagnoses; the nurses recorded the doctor's diagnosis and there were no explicit criteria for the different diagnoses. In addition, it is possible that a diagnosis has been set after decision on treatment, in a manner to justify the treatment, which would lead to an underestimation of 'outside guideline' antibiotic use [22]; 2) difficulties in assessing the appropriateness of the prescribing of individual cases; 3) lack of evidence-based guidelines for treatment of infections in the elderly in general, and in nursing homes in particular; as there was no document containing official national, consensus guidelines on antibiotic use in nursing homes, the research group reviewed and discussed the available guidelines for outpatients in general and eventually consented to a proposal of antibiotic guidelines for UTI, skin and soft-tissue infections and pneumonia. The acknowledged guidelines were mainly based on current national and/or regional recommendations and/or material from STRAMA, Swedish Medical Products Agency, Apoteket AB, Svenska infektionsläkarföreningen (Swedish Association for Specialists in Infectious Diseases) and local Drug Therapeutic Committees.

There is a need for updated, nationally accepted guidelines for the treatment of the most common infections in nursing homes. Special attention should be given to the treatment length for UTIs and the possibly irrational use of quinolones and doxycycline. The high proportion of antibiotics issued during indirect contact with the physician raises some concern about the management of infections in the elderly, and stresses the need to involve the nurses in education on antibiotic treatment as well.

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III

Urinary tract infections and antibiotic treatment in Swedish nursing homes.

A study on nursing assistants', nurses' and general practitioners' perceptions

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Abstract

Background: Urinary tract infection (UTI) is a common indication for antibiotic treatment in the nursing home setting, but the role and responsibilities of the different categories of staff in the prescribing process of antibiotics needs to be further explored.

Objective: The aim was to explore experiences and perceptions of the nursing home staff about urinary tract infections and their part in the antibiotic prescribing process.

Methods: Mixed methods design. The qualitative part was five focus group discussions (FGDs) with 10 nursing assistants, 10 nurses and six general practitioners (GPs) with experience from nursing homes. The focus group discussions were tape-recorded and transcribed verbatim. The data was analysed by content analysis influenced by the framework approach. The quantitative part was a knowledge- and attitude questionnaire about UTIs. 163 of 165 nurses and 35 of 41 GPs responded to the questionnaire when they took part in an intervention study about infections and antibiotic prescribing in nursing homes. The questionnaire was used as method triangulation for the FGDs.

Findings: The theme that emerged was "Interpersonal relations, timing and setting – the main determinants for management of UTIs and antibiotic prescribing in nursing homes." The categories that were discerned during the analysis were: "Symptoms of urinary tract infections – clinical signs and attitudes"; "What leads to antibiotic prescribing"; "Communication between the staff concerning infectious symptoms" and "Hygiene in the nursing home setting". This expresses that collaboration, communication, when the infection occurs, organisation and location have a perceived impact on the decision making process in the management of UTI in the nursing home.

Background

Urinary tract infections, UTI, are one of the most common indications for antibiotic treatment in the nursing home setting (Nicolle *et al.* 1996, Loeb *et al.* 2001, Blix *et al.* 2007, Pettersson *et al.* 2008). Inappropriate antibiotic prescribing concerning UTI has been shown, which could lead to negative consequences in form of bacterial resistance, which can render previously treatable infections untreatable (Jones 1987, Nicolle 1996, Takahashi 2004). Antibiotics are often prescribed for non-specific indications (Boscia and Kaye 1987, Nicolle 2002) although no relationship between bacteriuria and symtoms such as anorexia, fatigue, malaise or weakness have been shown (Warren *et al.* 1991). Difficulties encountered by the

nursing home staff in management of UTI in the elderly are mainly related to difficulties in eliciting information about symptoms because of cognitive impairment (Juthani-Mehta 2007). Presence of incontinence is also frequent which further complicates a diagnosis (Offermans 2009, Omli 2010). The presentation of symptoms in the elderly also seems to be different from symptoms in younger adults (Gavazzi and Krause 2002). A high prevalence of asymtomatic bacteriuria, which should not be treated with antibiotics, also adds to the picture of complexity, which gives urinary dipsticks low positive predictive value in this population (Nicolle 1993, Hedin 2002, Arinzon *et al.* 2009). Consequently, the predictive value of bacteriuria in residents with fever, without catheter, is only 10 percent (Orr *et al.* 1996). Pyuria, which is present in 90 percent of those with bacteriuria is not a predictor for symtomatic UTI (Boscia *et al.*1989).

There has been a decrease in persons from 65 years in Sweden, who live permanently in special forms of housing, including nursing homes, from 115 000 (7.5%) in 2002 to 95 400 (5.7%) in 2009 (SOS 2011). A reform was introduced for geriatric care in 1992 leaving the responsibility of geriatric long-term care to the municipalities instead of the County Councils, that are responsible for all other outpatient and inpatient care. The categories of health care staff in nursing homes are nursing assistants, nurses and general practitioners. The main tasks for the nursing assistants are: caring, housekeeping, medical, social and administrative tasks and social pedagogy (SOS 2006). The situation for the nurses changed after the reform from work in close collaboration with the general practitioner to work mainly on their own with responsibility for a large number of patients (Kapborg and Svensson 1999). Nurses are not formally authorised to prescribe antibiotics for systemic use. Although The National Board of Health and Welfare have descriptions of the competence required for registered nurses, RNs, there are no clear national definitions of functions and tasks for RNs in municipal elderly care (Svensson 2002) and there are only a few studies on their work situation in Sweden (e.g. Josefsson *et al.* 2007). General practitioners are not employed by the municipalities and the County Councils are responsible for all health- and medical care provided by the general practitioners (Akner 2004).

The role and responsibilities in relation to antibiotic prescribing among the different categories of staffs present in the nursing home needs to be further explored and defined.

The main aim of this study was to explore experiences and perceptions of the nursing home staff about urinary tract infections and their role in the antibiotic prescribing process.

Methods

A mixed methods design was chosen (Onwuegbuzie and Teddlie, 2003). Mixed methods research has been defined by Tashakkori and Creswell (2007) as "research in which the investigator collects and analyzes data, integrates the findings, and draws inferences using both qualitative and quantitative approaches or methods in a single study or a program of inquiry".

FGDs were chosen as the qualitative approach. FGDs captures interaction between participants in a way that individual interviews do not. Similarities and differences in views among the participants become more apparent through the interpersonal communication in the group (Freeman 2006). As statistical representativeness is not the aim of focus group research, a purposive sampling model was chosen (Kitzinger 1995). The participants were chosen to represent the different categories of health care staff working in nursing homes i.e nursing assistants, nurses and general practitioners. In order to be able to share their experiences one requirement for the participants was that they needed to have some practical, own experience from working in nursing homes. Each focus group was chosen to be homogenous to encourage mutual interaction during the sessions (Kitzinger 1995, Freeman 2006). Participants were recruited from nursing homes in two municipalities in the northern part and one municipality in the southern part of Sweden. In the written invitation participants were told that the purpose of the meetings was to discuss the role of the staff in management of infections in residents and to discuss about experienced infectious cases. The focus groups were held in settings where the participants felt comfortable to talk.

EP is a pharmacist by profession, CL is a research nurse, SF is a social scientist with a PhD in Public Health and CSL is a pharmacist and professor and research group leader for Medicines in the Health System – focusing antibiotics at Karolinska Institutet. The moderator, EP, used a written discussion guide with open-ended questions, developed by EP and the research group. The semi-structured guide also included probe questions to be used by the moderator if the discussion faded. The main items were "infections and elderly", "difficulties in treating UTI in elderly", "hygiene" and "management of infections – anything you wish to change in your nursing home?". The role of the moderator was to encourage all participants to share their

views, listen and to use exploratory probing questions (Murphy 1992). One observer took notes during the discussion to capture the atmosphere and expressions. The discussions were audio taped and then transcribed in verbatim by two assistants. The transcripts were checked against the audiotape by EP.

The data was analysed by content analysis influenced by the five different stages in the framework approach (Ritchie and Spencer 1993). 1) *Familiarisation* by listening to the tapes, reading the whole transcripts and the observational notes several times and making own notes in the material 2) Identifying a *thematic framework* by noting key issues and referring to the a priori aims of the study 3) *Indexing* all the data by noting parts with the same content in the margin 4) *Charting* by cutting and pasting and colouring the parts with similar content that was indexed in the previous stage from different FGDs (decontextualisation) 5) *Mapping and interpretation* where focus went back to the aim and once again the data was interpreted as a whole. The theme emerged from reading the transcripts interpretively over and over again looking for an essence in the material (Morse J, 2008). The last step could also be seen as a form of recontextualisation – to ensure that the categories and patterns that have been derived from the data still agreed with the context from where they were collected. Considerations have been taken to extensiveness of comments concerning a topic and negative cases i.e. an effort to find elements in the data that do not support or even contradicts the patterns found.

The quantitative part of the study was a questionnaire, which focused on knowledge and attitudes about UTI and its treatment. This questionnaire was sent to 165 nurses and 41 GPs at nursing homes that participated in an educational intervention study concerning infections in nursing homes (Pettersson *et al.* 2008). The sample for the questionnaire was thus completely separate from the focus group participants. 163 nurses and 34 GPs responded anonymously to the questionnaire. The relevant parts for this paper was collected during the baseline phase of the intervention study and included i) four dichotomous statements - true or false ii) Two four-point Likert scale statements – graded from totally agree to totally disagree. The statements are added to the information obtained from the focus group discussions as a method triangulation to increase the credibility and thus trustworthiness of the study (Lincoln and Guba 1985).

The collection and analysis of the qualitative and quantitative data were carried out separately and the results were related to each other during the interpretation of the findings.

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Findings

Five FGDs were performed: two with five nursing assistants; two with five nurses; and one with six GPs, table 1. The first three took place during 2003 and the last two during 2004. All participants had experiences from working in nursing homes. Table 2 presents an overview of the results from the quantitative questionnaire. The quantitative data has been related to the corresponding findings from the focus group discussions and are presented together with the qualitative findings below.

The main theme that emerged from the focus groups was: "Interpersonal relations, timing and setting – the main determinants for management of UTIs and antibiotic prescribing in nursing homes."

Interpersonal relations refer to the relationship, communication and interaction between the members of the staff and relations between the staff and the resident and their relatives. Social factors that were addressed during the focus group discussions were colleagues behaviour, which was described both as perceived actual and perceived ideal behaviour by many examples. Both general practitioners and nurses described a pressure to act upon the information given to them from other staff members, residents or relatives and sometimes this pressure was specifically a demand for antibiotics. Whether you know the patient or staff that you were communicating to was mentioned as important factors for your own action.

Timing refers to when the change in health status occurs, which could have perceived consequences for the actions taken.

Setting refers to organisational and structural factors of the nursing home for example availability of dipsticks, disinfection alcohol and location such as proximity to health care centers/GPs. Nursing assistants described organisational problems to comply with hygiene guidelines, such as availability of working clothes, disposable aprons, gloves etc. This was also sometimes referred to as economic factors i.e. priorities done by the managers of the nursing home units. The reform was only mentioned in a positive way by the GPs who meant that it improved the availability of nurses at the nursing homes, although the GPs themselves perceived that their own hours dedicated to nursing homes decreased.

The categories that were discerned during the analysis of the focus group discussions were:

- Symtoms of urinary tract infections – clinical signs and attitudes
- What leads to antibiotic prescribing?
- What does a positive dipstick or positive urine culture mean?
- Communication between the staff concerning infectious symptoms
- Hygiene in the nursing home setting

These categories are described below and followed by citations from the participants, where NA is nursing assistant, N is nurse and GP is general practitioner. NA 4C is thus interpreted as Nursing assistant C in focus group number 4 (chronological order).

Symtoms of urinary tract infections – clinical signs and attitudes

All groups described the multifaceted picture of symtoms of urinary tract infections in the nursing home setting. Interpretation of non-specific changes in health status can be difficult because of cognitive impairment in the nursing home residents. The symtoms range from specific clinical urinary tract symtoms such as urgency, frequency and dysuria to non-specific signs as foul-smelling urine, confusion, falling, aggression and agitation.

”Many of our elderly they don’t react with fever, they just fall or get confused. It is other symptoms.” [N 3F]

”we have a lady who /…/ sees dogs and cats around her bed. /…/ and that is the first sign – so there is nothing else to do but prescribe antibiotics.” [N 5E]

“...well, I had one who always started singing (the children’s song) *Baa Baa Black Sheep*”. [NA 4C]

They all described differences in management of these different symptoms from GPs treating merely all conditions to other GPs with a more restrictive attitude towards treatment.

”We have got the answer (from the GP) that: - I don’t treat foul-smell”. [N 3B]

”The staff usually came to me and said: -Now we have to treat with something because there is foul-smelling urine. At the hospital we had a GP, who used to say: -Is it the patients or the staff we should treat?” [N 5E]

The presence of non-specific symptoms, sometimes as the only sign of UTI, was also supported in the questionnaire, table 2, statement 1 where 94% of the GPs and 90% of the nurses agreed to that confusion can be the only sign of an UTI in the elderly.

What leads to antibiotic prescribing?

Fever is naturally a trigger for antibiotic prescribing. However, 97% of the GPs and 85% of the nurses did agree that fever does not *have to* be present to prescribe antibiotics (table 2, statement 2). Influences from other members of the staff and residents’ relatives to take urine samples and to treat with antibiotics are experienced in different ways.

“It is easier to wait and see if you know the persons involved than if the GP is completely unknown to the nurse, the residents and the relatives. Then it is easier just to prescribe.” [GP 2D]

“It is easier to ‘wait and see’ if they call a Sunday night than if they call a Friday night – then you prescribe antibiotics.” [GP 2F]

The nurses have a gatekeeping role concerning inititation of treatment of infections in the nursing home setting. This is acknowledged by all groups although the general practitioners refer to it as a middle role between the nursing assistants and the general practitioners. The GPs did not see this role as a problem as long as there is a concensus between the different categories of staff on how to manage infections.

“I believe that a nurse that wants the patient to get a treatment achieves this by describing (the symtoms/health status) in a certain way. I am totally convinced. This is part of the interplay we have – nothing strange with that, really.” [GP 2B]

This might however be a problem when there is temporary staff involved as there seem to be differences in how the staff acts if they know the people involved.

”Well, it is even so that you prescribe antibiotics by phone if they say that there is a foul-smelling urine and fever.” [GP 2 F] ”…but the difference is that it is easier to wait and see or refrain from treatment if you know somebody than if a total stranger, maybe both the patient, the nurse and relatives are strangers (to you) /…/.” [GP 2D]

”If you call the on-call duty and bring out the problem, you will get what you want.” [N 5B]

In contrast to the FGDs neither the nurses nor the GPs acknowledged the nurses as having a key role in the antibiotic prescribing process in the quantitative questionnaire. 56% of the GPs and 73% of the nurses totally disagreed to the statement that the nurse decides when to treat an UTI, table 2 statement 5. 82% of the GPs and 91% of the nurses totally disagreed to that the nurses decides the type of antibiotics, table 2 statement 6.

What does a positive dipstick or positive urine culture mean?

Both the nurses and the GPs discussed about asymptomatic bacteriuria (ABU) while the nursing assistants did not. The general practitioners are the only ones actually referring to it as ABU. The nurses sometimes referred to it as silent UTI and agreed that this should not be treated with antibiotics. The magnitude of the problem and how to handle it is unclear, especially in diabetic patients. In practice it seems to be handled differently in different nursing homes. To decrease the number of urine samples taken, the nursing assistants do not have free access to dipsticks - it is sometimes kept in the nurses’ office.

”Is it a UTI just because the patient has fever and positive nitrite when you know that maybe half (of the residents) have positive nitrite?” [GP 2E]

”…but there are many saying that there is a very high percentage in elderly who has positive nitrite no matter if they are ill or not. ” [GP 2A]

”…and the silent urinary tract infections we do not treat.” [N 3E]

The opinion that bacteriuria should not always be treated, was supported in the quantitative questionnaire of 91% of the GPs and 86% of the nurses, table 2, statement 3. This also points out that GPs and nurses have knowledge about the existence of ABU in the elderly. 76% of

the GPs and 74% of the nurses also agreed that fever and symptoms of UTI is an indication for urine culture, table 2, statement 4.

Communication between staff concerning infectious symptoms

The communication between members of the staff was widely discussed during the sessions. Nursing assistants described a perceived ideal situation as beeing part of the team as they are the ones knowing "their" residents. However, the real situation is different and they can rarely have a direct communication with the GPs. Both GPs and nurses describe a pressure from the nurses and nursing assistants respectively, or relatives to prescribe antibiotics or at least act in some way on the information provided to them. Whether you know the patient or staff that you were communicating to was mentioned as important factors for your own actions.

"The only one we talk to is the nurse, so we don't have any contact with the GP. We talk to the nurse and then I expect that she forwards these thoughts." [NA 1D]

"It is very different between different GPs. Some GPs treat everything so you hesitate (to contact them). If they do not have that many symptoms you can wait and see and give something to drink." [N 5D]

The GPs also described the communication:
"So you describe a system where a nurse who doesn't know the patient calls the GP, who doesn't know the patient, who chooses to treat the patient without seeing the patient". [GP 2B] "Yes, that is an optimal situation (irony)". [GP 2A]/.../

They were continuing their discussion on when to go to the nursing home and conclude that there are many determinants for when to and when not to go to the nursing home.

"There are many factors /.../ . [GP 2B] "But if they call about a patient with positiv nitrite, some fever and foul-smelling urine - you wouldn't get that much wiser by going there to see them." [GP 2A] /.../

[GP 2A] and [GP 2B] agreed that if it is another kind of infection, where there could be differential diagnoses, they should go and see the patient.

The GPs seemed to wish for a consensus from the nursing home before the nurse contacted them so that the GP did not get several different stories.

"Some people exaggerate very much and others you know that when they say something it really means something, but it takes time to get to know the staff at the nursing home I have. I mean there is a staff - well I don't know how many but I think there are 70-80 people working there during daytime." [GP 2D] "/.../ because the nurse is usually in a middle function who is also dependent on what the nursing home staff reports." [GP 2B] "/.../ but in practice it is impossible in a nursing home that there is a crowd with nursing assistants outside waiting to come in one after the other every time there is a new question. It simply doesn't work." [GP 2A]

When the GPs talked about the communication with the staff at the nursing home they agreed with the following GP that: "It is important that the staff at the nursing home agree and provide us with one picture instead of calling us and presenting two different ideas /.../." [GP 2D]

Hygiene in the nursing home setting

The groups with nurses and nursing assistants all seemed to be aware of the importance of correct hygiene practices. It is noteworthy how little the GPs talked about hygiene. Although there was awareness about hand hygiene there were practical problems mentioned remaining such as the many tasks for the nursing assistants.

"We are dealing with garbage and wounds during the same day wearing the same clothes." [NA 1B]

All groups but especially the nurses described the conflict between the nursing home being a home for these very old, frail and multiple ill patients and at the same time the need to provide high quality of care. Critique against the reform was constantly woven into the discussions about hygiene expressed for example by a nurse assistant in focus group 4:

"And now, you are not wearing your working clothes at home, but I wear them when going home. That was absolutely unthinkable before (the reform) /.../ but now we have built up this new nice own-home-living home-environment and all. Then you start to wonder due to their

(the residents') bad condition when they come here – are we going back to all that again. /.../ Back to when we had working coats, but now we need to integrate so it won't show whether we are staff or relatives." [NA 4B]

"And then we go, wearing the same clothes as we had in the room with the one with stomach disease, to the dining room and serve them a meal there." [NA 4D]

"It has to be home-like living, but with certain additional items based on the needs, looking after (the residents) and so on. Otherwise it is kind of pointless having staff." [N 5A]

Discussion and methodological reflection

The theme "Interpersonal relations, timing and setting – the main determinants for management of UTIs and antibiotic prescribing in nursing homes" expresses the latent content in the FGDs. The management of UTIs seems to be very dependent on who is involved in the process and how this is organized. Who is the nursing assistant, who is usually the first to observe the resident's change in health status? Who is the nurse to whom the nursing assistant reports to? Who is the GP to whom the nurse reports to? Are they familiar with the resident and relatives to the resident? Have they been working together for a longer period of time? Where is the GP located? And eventually, what day of the week is it and what time is it when this change in health status is reported?

Professional interpersonal relations is similar to the definition of collaborative practice provided by Way *et al.* 2000: "Collaborative Practice is an inter-professional process for communication and decision making that enables the separate and shared knowledge and skills of care providers to synergistically influence the client/patient care provided." From our FGDs we also would like to add the interplay between the staff and the residents and relatives into the discussions about collaboration in the nursing homes. Collaboration, in particular between nurses and physicians, has been vastly studied in the literature but has mainly focused on collaboration itself and not the impact on outcomes of interests (Donald *et al.* 2010). In 2000, Zwarenstein and Reeves made an editorial in BMJ about the lack of evidence within the research field on collaboration and in 2009 they and Goldman J made an updated Cochrane review about practice-based interventions to change interprofessional collaboration, IPC (including randomised controlled trials to 2007). They suggested that practice-based IPC interventions could have a positive impact on processes and outcomes in healthcare, but the

review was only based on the five studies that met the inclusion criteria. They also stated that research within the field of IPC is complicated due to differences in terminology. Kvarnström *et al.* 2008 meant that health care professionals consider that difficulties in IPC could lead to perceived consequences in form of problems to provide the desired patient care. From prescribing practices in the long-term care setting it has been shown that poor collaboration between physicians and nurses was perceived as a barrier to optimal pain management (Kaasalainen *et al.* 2007).

Timing of the infection can affect the management according to the participants in the FGDs, but no evidence that would support that the on-call duty's prescribing is different from the ordinary GP's or that prescribing of antibiotics would be more frequent on Fridays than any other day of the week is available in the literature.

That the setting makes a difference has also been indicated in a study from Boston, USA, on gerontological nurse practitioners perspectives on prescribing (Mahoney and Ladd, 2010). They included examples such as location of the patient and that nurses chose to work in places where the physicians were supportive.

The categories represent the manifest content in the material. While interpreting the findings, attention was given to the picture provided by the group and an effort was put into distinguishing between opinions expressed in consensus within the group and opinions expressed in opposition within the group. It became clear that the participants in the focus groups experienced the nursing home setting in different ways. The nursing assistants talked about "their" residents and that it is important to care for them. Both nurses and GPs showed a more medical/clinical attitude towards the nursing home residents, which is probably due to the organisation of elderly care in the nursing homes and that the GP act as a consultant.

The description of symptoms of UTI in the elderly residents in nursing homes, ranging from the classic to the more non-specific signs, is in line with earlier results from FGDs with GPs and nurses in Canada (Walker 2000). However, the literature does not support prescribing of antibiotics on these non-specific symptoms (Boscia and Kaye 1987, Nicolle 2002, Warren *et al.* 1991).

The key role of the nurses in the prescribing process of antibiotics in nursing homes described here have also been shown in Walker *et al.* 2000 and Loeb *et al.* 2005. The participants described a gatekeeping role both in terms of access and monitoring of others action. We do not intend to present an opinion on how the practice should be, but we believe it is important to acknowledge this situation and make policy decision from this stand point. If this is how the policy makers intended it to be, it is time to involve the nurses in nursing homes in more educational activities concerning infections and antibiotics and if this is contrary to the policy makers' views, it is time to act upon that.

ABU was known to different extent in the different FGDs. In some of the groups there was an uncertainty about the prevalence of ABU and how to manage it practically. The high prevalence of ABU in the nursing home population (Nicolle 1993, Hedin 2002, Arinzon *et al.* 2009) and low predictive value of bacteriuria and pyuria for UTI need to be further communicated to the staff in the nursing homes (Orr *et al.* 1996, Boscia *et al.*1989). Standard screening test for bacteriuria and pyuria i.e. dipstick tests can be helpful for excluding UTI but not to confirm UTI in this population.

The participants in all FGDs described communication with each other and with the residents and relatives. Relations, interaction and communication seem to play an important role in the management of infections. To our knowledge there are no studies focusing on the professional communication between nurses and nursing assistants in long-term care facilities. There have been studies on the nurse-physician communication in long-term care facilities (Cadogan 1999, Kayser-Jones 1986 and 1989, Perkins 1993) and at least one focusing on telephone communication, although only including nurses (Tjia 2009). Barriers to communication found by Tija 2009: openness/collaboration, logistic challenges, professional respect/frustration, language/mutual understanding and nurse preparedness, can also be found in this study although they are exemplified in different ways in our FGDs. Schmidt *et al.* 2002, conducted a study in nursing homes in Sweden on communication and quality of prescribing with a focus on psychotropic drugs, where it was noted that the quality of drug use was positively associated with both the quality of nurse-physician communication and with regular multidisciplinary team discussions about drug therapy. The same correlation could possibly be expected also for antibiotics.

The terminology for evaluative criteria in qualitative research is a little bit different both compared to quantitative research but also within qualitative research depending on the research tradition. Lincoln and Guba 1985, offers a theoretical framework where they mean that trustworthiness is established through credibility (internal validity), transferability (generalisability or external validity), dependability (consistency) and conformability (researcher bias and reflexivity). Other researchers such as Malterud 2001, who provides a comprehensive guideline for authors and reviewers within qualitative research, Mays and Pope 2000 and Graneheim 2004 have similar criteria for validity in qualitative research but the presentation differs.

As this was an exploratory study, combining the descriptive results from the questionnaire with results from the focus groups, the findings are hypothesis generating rather than evaluative. Because the participation was voluntary the findings might only reflect opinions from those concerned in the area of infectious diseases. For our purpose it was important that all participants had substantial working experience from nursing homes. This could, however, have had an impact on the findings as the views can be different depending on years of experience. In addition we have not used observations, which mean that we do not have information about the actual behaviour; only how it is perceived by the staff represented in these focus groups. Some of the quotations also describe a perceived ideal behaviour.

To increase credibility two types of triangulation was used: investigator or analyst triangulation and method triangulation. Both EP and CL has read and analysed the whole transcripts independently of each other and then discussed it in the research group to minimise interpretive bias of the findings (Patton 1999). Although integration of qualitative and quantitative data has been widely debated in social science, there can be advantages of combining the two on a chosen level (Onwuegbuzie and Teddlie, 2003). Ostlund *et al.* 2011 implicated that mixed methods and triangulation can help the researchers within nursing- and health sciences to clarify, understand and make valid inferences of their results, although they acknowledge the presentation of mixed methods as challenging. The method triangulation provides means both for the researcher and the reader to make conclusions based on the two different methods. When the methods show confirmative results it does help to establish the credibility, but where the results diverge, an interpretation of the results are more difficult to make. For example the participants in the FGDs pointed out that the nurses have a key role in the antibiotic prescribing process, which was expected as it has been shown that the GPs in

38% of the times when an antibiotic is prescribed are not present at the nursing homes (Pettersson 2008). This was not supported in the questionnaire. However, the questionnaire did not allow elaborated answers, while the whole purpose of FGDs is to discuss and get as many views as possible. Here one needs to make a choice on which method is most valid for this particular question. We chose to emphasis the qualitative method here, but for other kinds of questions the correct choice might not be obvious.

A negative- or deviant case analysis was also made to try to find elements during the discussions that did not support the emerging patterns, categories and themes. From the beginning there were more categories and examples of themes, which could be reduced after a more thorough analysis. The participants seemed comfortable with the choice of location for the focus group discussions and did not show any signs of not wanting to share their experience with us. Those who accept an invitation to participate in a focus group are probably more prone to tell their story then those that decline such an offer, which per se could limit the transferability of the findings. The geographical areas chosen for these FGDs and the fact that the participants had experience from municipality owned nursing homes could also have limitations on the transferability to metropolitan cities and privately owned nursing homes. With the data collected during a longer period of time, there was a risk for inconsistency in the data collection, but a shift in content of the FGDs was not noted and the same discussion guide and the same moderator was used for all sessions.

Conformability is referring to in what way the researcher and research process have shaped the data. Malterud 2001 and Mays and Pope 2000, have among other researchers acknowledged that reflexivity, or how researcher perspective and position, influence the research process, interpretation, findings and conclusions and suggest means to address this. The method- and analyst triangulation and the description of the researchers' professional background are means to make the presentation of the analysis more transparent to what might have had an influence on the data.

In this study it was not possible to have the same sample in the focus group and the intervention study, from where the quantitative data was collected, as it could have affected the results of the intervention study, but for future research it would be interesting to see how interpersonal relations and communication correlates to the quality of antibiotic prescribing.

Conclusions

Interpersonal relations between the staff, residents and relatives, timing i.e. when the infection occurs and setting i.e organisation and location are perceived by the nursing assistants, nurses and GPs to be the main determinants in the management and antibiotic prescribing for UTIs in nursing homes. The nurses' gatekeeping role in the prescribing process needs to be further explored and evaluated in order to effectively and in a patient safe manner manage UTIs in the nursing homes.

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Table 1: Focus group sample

Group	Category of staff	Number of participants and sex	Age range	Location
1	Nursing assistants	5F	35-48	Norrbotten County
2	General Practitioners	1F, 5M	43-52	Jönköping County
3	Nurses	5F	52-61	Norrbotten County
4	Nursing assistants	5F	35-60	Norrbotten County
5	Nurses	5F	53-59	Norrbotten County

Total participants = 26 (21F 5M)

Table 2: Results, in numbers, from a knowledge and attitude questionnaire with 163 nurses and 34 general practitioners, GPs.

Statement	Profession	Missing	True	False	Do not know
1. Confusion can be the only symptom in elderly with UTI	GPs Nurses	0 1	32 147	1 15	1 0
2. Fever is always present in UTIs that should be treated with antibiotics	GPs Nurses	0 0	1 21	33 139	0 3
3. Bacteriuria should always be treated	GPs Nurses	2 3	0 11	31 140	0 4
4. If the resident have fever and symptoms of a UTI you should do an urine culture	GPs Nurses	3 8	26 121	5 36	1 3
			Totally disagree	**Disagree in many cases**	**Agree in many cases**	**Totally agree**
5. In practice, the nurse decides whether or not to treat an UTI	GPs Nurses	1 2	19 119	7 22	6 12	1 8
6. In practice, the nurse decides which type of antibiotic that is prescribed for an UTI	GPs Nurses	0 3	28 148	4 8	1 3	1 1

IV

Can a multifaceted educational intervention targeting both nurses and physicians change the prescribing of antibiotics to nursing home residents? A cluster randomised controlled trial.

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Abstract

Objective To assess the impact of a multifaceted educational intervention concerning treatment of infections in the nursing home setting.

Methods Cluster randomised controlled trial. 58 nursing homes in Sweden were randomly assigned either to educational intervention or control. The intervention consisted of small educational group sessions with nurses and physicians, feedback on prescribing, presentation of guidelines and written materials. Primary outcome was proportion of quinolones prescribed for lower urinary tract infection, UTI, in women. Secondary outcomes were for all infections: number of UTIs per resident, proportion of recorded infections treated with an antibiotic, proportion of infections handled by physicians' "wait and see"; and for lower UTI in women: proportion of nitrofurantoin.

Results Of the 58 nursing homes, 46 completed the study. 702 and 540 infections were recorded pre- and post-intervention. Proportion of quinolones decreased significantly in intervention- and control group by -0.196 and -0.224 respectively (95% CI -0.338 to -0.054 and -0.394 to -0.054) but the difference between intervention and control was not significant 0.028 (95% CI -0.193 to 0.249). The changes in proportion of infections treated with antibiotics and proportion of infections handled by physicians' "wait and see", was significant in comparison with controls: -0.124 (95% CI -0.228 to -0.019) and 0.143 (95% CI 0.047 to 0.240). No intervention effect could be seen for the other outcomes.

Conclusions The educational intervention had no effect on the primary outcome, but decreased the overall prescribing of antibiotics.

Trial registration number: NCT01054677 at http://www.clinicaltrials.gov/

Introduction

Inappropriate use of antibiotics is still a common problem in the nursing home setting [1-4] and can lead to adverse events for the consumers [5], development of resistance [6-8], increased mortality [9] and also excessive costs for the care providers [10]. To address the problem of inappropriate prescribing, a multi-faceted educational intervention was developed. The main focus was on antibiotic treatment for lower urinary tract infection, UTI, in women, as it is the main indication for antibiotic treatment in nursing homes.[3] Traditionally, physicians have been the target group for interventions concerning prescribing practices for urinary tract infections in outpatient care.[11-13] However, as it was known that 38% of antibiotic treatment in nursing homes was initiated without direct contact with the physician, we decided to include the nurses in the intervention as well although they are not formally authorised to prescribe antibiotics for UTI.[1] This was also supported in Loeb M et al, 2005.[14] Changing professional practice is difficult and there is no universal recipe for success, but reviews suggest that multi-faceted, active strategies have a higher likelihood of success than single interventions.[15-16]

The aim of this paper is to present the evaluation of a multifaceted educational intervention on change in a predetermined set of outcomes concerning infections in the nursing home setting.

Material and Methods

We have adopted the CONSORT statement for reporting randomised controlled trials.[17-18] Additional information required for cluster randomised trials has also been reported in accordance with the extension to the CONSORT statement 2001, expressed in Campbell et al 2004.[19]

Design

This study is a cluster randomised controlled intervention study with two study arms i.e. intervention and control (figure 1). The nursing home was the unit of allocation and intervention, but in the analysis individual resident data was used allowing for clustering on the nursing home level.

Participants/setting

The research coordinator sent an invitation letter to all nurses charged with medical responsibility within local authority elderly care in Sweden, enquiring about participation in the study (n=366 at the time of invitation). The inclusion criteria were nursing homes where residents have a common dining room and staff, and a self-assessed stable staff situation. Exclusion criteria were specialised nursing homes or wards (e.g. oncology wards). For a flowchart of the trial, see figure 1. A pilot study including seven nursing homes preceded the trial. The aim of the pilot was to optimise the instruments and educational intervention and to enable us to do a sample size calculation. Nursing homes from different parts of Sweden were included in the main trial. Data from the pilot study was not included in the analysis of the main trial.

Sample size calculation

The number of clusters needed was calculated [20] as 25 in each arm to have 90% power to detect a 20% relative difference in prescribing of quinolones ($\alpha = 0.05$), assuming a baseline rate of 4.5% quinolone users based on the pilot study and literature, average cluster size of 60 residents, and a intracluster correlation coefficient, ICC, taken from literature of 0.05.[21-22]

Data collection and outcomes

During three months from September 15 to December 15, 2003 we collected baseline data. The parts of the trial relevant to this paper were: diagnosis-prescribing survey, (DPS) and a nursing home questionnaire (NHQ). For the DPS, the nurse responsible was requested to fill in a form for all patients with infectious symptoms requiring a physician's opinion. Recorded information included patient age, sex, indwelling urinary catheter i.e KAD; if physician was present at the nursing home; the main infection, antibiotic treatment if prescribed, type of antibiotic and treatment length and factors influencing the choice of treatment or referral of the patient. If a resident had several diagnoses on one occasion, one form for each infection was recorded. As the purpose was not to assess the risk for infections in nursing homes, but to present changes in the prescribing pattern, recurrent infections were included. We focused on a predetermined set of outcome variables as indicators for a possible change. Proportion of quinolones for lower UTI in women was the primary outcome. Secondary outcomes were number of UTIs per resident; and for all infections: proportion of infections treated with antibiotics, proportion of infections handled by physicians' "wait and see"; and for lower UTI in women: proportion of nitrofurantoin. The proportion of admissions to hospital was presented as an indicator for the adverse events of the intervention. The NHQ was used to collect information on the nursing homes, as specified in table 1. Intervention was conducted from October 25, 2004 to January 21, 2005. From February 14 to May 16, 2005 we collected post-intervention data by using the same instruments as for baseline data collection. DPS and NHQ were repeated for the nursing homes and the results were compared with the baseline results.

Table 1. Characteristics of intervention versus control nursing homes included in the analysis of the intervention effect, at baseline. 95% CI is presented.

	Control nursing homes	*Intervention nursing homes*
Number of included nursing homes	20	26
Number of residents	1143	1394
Mean number of residents/nursing home	57.2 (37.1-77.3)	53.6 (37.2-70.1)
Age, mean	83.7 (82.6-84.9)	83.9 (82.0-85.8)
Proportion of females	0.67 (0.64-0.71)	0.69 (0.64-0.74)
Proportion UTI/ residents	0.15 (0.13-0.17)	0.14 (0.12-0.16)
Antibiotic courses per resident and year, mean	1.11 (0.13-2.10)	0.97 (0.14-1.79)
Proportion of residents with indwelling urinary catheters	0.08 (0.05-0.11)	0.07 (0.04-0.10)
Proportion of residents immunised against influenza	0.73 (0.61-0.85)	0.65 (0.51-0.78)
Use of disinfection alcohol Litre/resident and month	0.19 (0.09-0.28)	0.13 (0.08-0.18)
Number of staff/resident		
Physicians (h/week/resident)	0.08 (0.06-0.10)	0.05 (0.03-0.07)
Registered nurses	0.08 (0.05-0.11)	0.08 (0.04-0.11)
Nursing assistants	0.77 (0.56-0.98)	0.67 (0.54-0.79)

Random assignment

In 2004, after the baseline DPS, the nursing homes were stratified into 3 equally sized groups based on the number of UTI/resident for each nursing home at baseline. To get a geographic spread of the intervention and control, the nursing homes were also divided into three geographical areas. The nursing homes within each of the nine final strata were randomly assigned to either intervention or control. EP performed a randomisation by computer where 50% in each stratum were randomly selected to comprise the intervention group.

Educational intervention

The description of the intervention have been influenced by the framework for describing the key features of a quality improvement intervention published by Hulscher et al 2003, see box

1.[23] The development of the intervention began with project group meetings, focus group discussions with physicians, nurses and nursing assistants working in nursing homes, and eventually evaluation of the intervention in the pilot study and revision before the main trial. In addition to feedback and references to available guidelines; structural, organizational and social barriers to change were discussed. Material for presentation was developed in the study group. To make the intervention more context-specific, the participating physician and hygiene nurse were local, and we also referred to guidelines from the local drug therapeutic committees.

Box 1. Educational intervention		
Main components of the intervention		
	-2 sessions of voluntary continuing medical education 1.5 h each	-2 to 3 external facilitators presented the guidelines and stimulated interactions between the participants: one pharmacist, one physician, and when possible a hygiene nurse. At least one of them was active in Strama-work.
	-Educational materials	-Leaflet on hygiene -Handouts during the sessions -Short written guideline for antibiotic prescribing
	-Feedback on performance	-Baseline results both written and verbal -Verbal summary at the end of the sessions
Main content of the intervention		
	-Feedback on baseline results -Guidelines on antibiotic prescribing for the most commonly encountered infections in the nursing home setting -Local pattern of antibiotic resistance	-The content of the intervention was presented both verbally and in writing.
Target group of the intervention		
	-Nurses and physicians at the included nursing homes. Ranged from 2-13 participants during the different sessions.	-The nursing home was the cluster and unit of allocation, intervention and analysis
Main outcome measures, proportions		
	1. quinolones for lower urinary tract infections, UTI, in women 2. UTI per resident 3. antibiotic prescriptions for all infections 4. physicians' "wait and see" for all infections 5. nitrofurantoin for lower UTI in women	
Evaluation of the intervention		
	- Differences before and after intervention for the main outcome measures.	-A written evaluation of the training was also completed after the sessions

Recommended treatment for UTI in women were at the time for the trial, pivmecillinam or nitrofurantoin for 5-7 days and trimethoprim for 3-5 days (note: national guidelines were

changed in 2007). For patients with KAD, quinolones for 10 days was the recommended treatment.

Statistical analysis

The nursing homes were analysed according to ITT with respect to allocation. However, a full application of intention to treat, ITT, analysis was not possible as complete outcome data was not available for all randomised nursing homes.[24] What separates the analysis from a true ITT is that the evaluation of the intervention has been done for the 46 nursing homes remaining at follow-up i.e an available case analysis. All questionnaires were sent to the coordinator for entering, and analysis of data using SPSS 17.0 (at start 10.0) software. For precision of measurement, the 95% confidence interval, CI, is presented both for baseline characteristics and the main outcome variables. After baseline, the actual ICC for each variable was calculated in SPSS according to the mixed effect model. For the primary outcome, the calculated ICC was 0.03. All figures describing the intervention effect are adjusted for the design effect, which was calculated for each outcome variable. Deff = $1 + (n - 1)\rho$, where ρ is the ICC.[25] A multivariable linear regression was performed in SPSS 17.0 to explore potential confounders: Residents' age, availability of physicians, nurses and nursing assistants, KAD, volume of disinfection alcohol consumed and special needs of the residents. Special needs of the residents were calculated as: $1/7 \times Hyg_{prop} + 1/7 \times Cloth_{prop} + 1/7 \times Mov_{prop} + 1/7 \times Toi_{prop} + 1/7 \times Eat_{prop} + 1/7 \times Press_{prop} + 1/7 \times Leg_{Prop}$. Hyg_{prop} is the proportion of residents not managing personal hygiene. $Cloth_{prop}$ is the proportion of residents not managing clothing. Mov_{prop} is the proportion of residents not managing moving around. Toi_{prop} is the proportion of residents not managing visits to the toilet. Eat_{prop} is the proportion of residents not managing eating. $Press_{prop}$ is the proportion of residents at the nursing home with pressure wounds. Leg_{Prop} is the proportion of residents at the nursing home with leg ulcerations. The choice of items was influenced by Katz ADL score, but dichotomised to independent or

dependent. Two additional items: pressure wounds and leg ulcerations were added.[26] We chose an equal weight to each of these variables in the calculation.

Ethical considerations

The research was conducted in accordance with the Declaration of Helsinki. The study was approved by the Regional Ethics Committee in Stockholm (dnr 03-070). The head of all units involved in the project, as well as physicians and nurses, were asked to give their written informed consent. The participation was voluntary i.e. only nursing homes where the staff agreed to participate were included. After the end of the trial the control nursing homes were invited to a similar educational session as that for the intervention homes.

Results

Baseline characteristics were similar for the intervention and control nursing homes (table 1). Antibiotic courses per resident and year; the immunisation rate; number of residents per nursing homes; the use of disinfection alcohol and availability of physicians and nursing assistants seemed a little bit higher in the control group, but all 95% CIs overlap. Of the original 58 nursing homes, 46 with a total of 2,511 residents remained at follow-up (figure 1). These nursing homes had at baseline 2,537 residents. Efforts were made to get details on the dropouts, but for three of them it was not possible. During the three months of data collections there were 702 infectious episodes recorded pre-intervention, compared to 540 post-intervention. According to the attendance lists 164 people were exposed to the educational intervention of which 13 were general practitioners.

For changes in the main outcome variables, see table 2. Proportions are presented with their 95% CIs. Discrepancies between the denominator for each proportion and the respective number presented for all infections and lower UTI in women are explained by missing values.

The proportion of the primary outcome, quinolones for lower UTI in women, decreased significantly in both intervention- and control group by -0.196 and -0.224 respectively (95% CI -0.338 to -0.054 and -0.394 to -0.054). The difference in change between intervention and control was not significant 0.028 (95% CI -0.193 to 0.249). The number of UTIs per resident decreased significantly in both intervention and control arm -0.031 and -0.070, but the change of 0.038 was not significant (95% CI -0.013 to 0.089). The proportion of infections treated with an antibiotic decreased significantly, by -0.124 (95% CI -0.228 to -0.019) in comparison with the control group. The proportion of infections handled by physicians' "wait and see", increased significantly in the intervention group compared with the control group by 0.143 (95% CI 0.047 to 0.240). The proportion of nitrofurantoin prescribed remained the same in both groups, before and after the intervention.

Parameter estimates for relevant explanatory variables in the multivariable regression on the primary outcome - proportion of quinolones for lower UTI in women: Intervention 0.163 (95% CI 0.026 to 0.301); physician-hour per week 2.178 (95% CI 0.357 to 3.998) and special needs 0.115 (95% CI 0.036 to 0.194).

Adverse events

There was no increase in admissions to hospital in the intervention group. The number of admissions in 2003 was 15/311 for the control group and 15/355 for the intervention group. In 2005 it was 5/203 for the control group and 20/299 for the intervention group. Change in control group -0.024, 95% CI -0.056 to 0.008 and change in intervention group 0.025, 95% CI -0.011 to 0.060.

Discussion

The educational intervention significantly changed the proportion in courses of antibiotics prescribed and it also influenced the proportion of infections handled by physicians' "wait and see". However, no intervention effect could be seen for the other outcomes including the primary outcome - proportion of quinolones prescribed for lower UTI in women.

By giving information e.g on the prevalence of asymptomatic bacteriuria in the nursing home setting, we hoped to reduce the proportion of residents diagnosed and thus treated for an UTI.[3,27] The educational intervention did not have the expected effect on this outcome. Availability of physicians could be a possible confounder. Sweden is a low-prescribing country with respect to antibiotics.[28] It was thus expected to influence the pattern of prescribing towards the guidelines but not to reduce the total use of antibiotics, although this is what we eventually did. In clinical practice the result in this context would mean a decrease of approximately 6 courses of antibiotics over one year in a nursing home with 50 residents. A comparison with results from reviews of intervention studies of antibiotic practices are difficult to make as the studies included in the analysis mainly target outpatients; one of the most common disease targets being respiratory tract infections, RTI .[15-16] Here the main indication is UTI, not RTI.

The significant and clinically relevant change in the prescribing of quinolones, the primary outcome variable, cannot be attributed to the intervention. Multivariable linear regression showed that the intervention influenced the prescribing of quinolones but availability of physicians, and special needs were potential confounders. Concerning the quinolones there has been a rigorous work of drug therapeutic committees and Strama, the Swedish strategic

programme against antibiotic resistance, to reduce prescribing where it is not indicated. As an example, between 2003 and 2005 the quinolones decreased from 173 to 149 prescriptions/1000/day in the age group 80 and over.[29] No significant increase of nitrofurantoin could be seen. In a study on outpatient prescribing of nitrofurantoin in 2000, 2002 and 2005 there was an increasing trend.[30] The total nitrofurantoin use increased from 27 prescriptions/1000/day in 2003, to 37 prescriptions/1000/day in 2005.[29] A secular trend in the outcome variable could thus explain the lack of significant results for the quinolones. For nitrofurantoin, where there were very few cases, it is likely that the study was underpowered to detect any possible differences. The results have been adjusted for clustering. The questionnaires had been tested for face validity and feasibility during the pilot study. The educational intervention and the working methods had also been tested in the pilot study. We cannot be certain that the participants in the intervention were the same as the evaluated group, as we did not collect information on the identity of the prescribers.

The modest effect of the intervention can have several explanations such as: i) low exposure to the intervention or that staff from two control homes also participated in the intervention, ii) a secular trend in the outcome variables. For feasibility reasons, the nursing homes did not receive the intervention at the same point in time and it was more than one year between the pre- and the post-intervention data collection. During this time there are changes in the nursing homes in staff and residents and factors outside the trial are given time to influence the outcomes. Contamination, which would dilute the intervention effect, also needs to be considered as nurses and physicians in one intervention home also could work in a control home. Hawthorne effect could also have affected the results if prescribing behaviour changed only because of the fact that the participants knew that they were being studied and not because of the intervention. For the quinolones this might have had an additive effect to the

secular trends described earlier. Seasonal changes in use of antibiotics are not likely to have an influence on the results in this trial as monthly sales statistics for ATC code J01 between 2002 and 2004 for elderly above 80 years only range from 39.1 to 43.3 DDD/1000 inhabitants. In addition the primary outcome for this trial concerned lower UTI in women and seasonal variations do not apply in a meaningful way to UTIs in this patient group. There was a wide geographic spread of nursing homes, which was desirable for high external validity, although this probably contributed to a higher dropout rate in our study. There were more dropouts in the control nursing homes and only 20 nursing homes remained for analysis, which raises the question of attrition bias. Experiences from the pilot study, where there were no dropouts, indicate that this difference could be explained by the absence of the coordinator in the control homes rather than that participants became weary of the study. An exploratory analysis at baseline showed that the outcomes in dropout nursing homes did not differ substantially to those of homes remaining during the whole trial (data not shown). Thus, the dropouts probably had little influence on the intervention effect.

The antibiotic prescription rate at baseline in the nursing homes in this trial was a little bit lower compared to earlier studies (1.0 per resident and year compared to 1.1 - 1.9).[1] This could be an indication of selection bias in the way that the nursing homes included in this study might be more interested in the area of infectious diseases and thus perhaps more restrictive to antibiotic treatment to begin with. It would then be difficult to show a statistically significant effect of an intervention as the changes would probably be small.

A review in 2006 of educational interventions targeting antibiotic prescribing behaviour (mainly for respiratory tract infections) showed a median absolute effect of -8.9%

(interquartile range, IQR -12.4% to -6.7%). When targeting selection of antibiotics, the included interventions were considered effective with a median absolute improvement in prescribing of recommended antibiotics of 10.6% (IQR 3.4% to 18.2%).[31] The effect of our intervention could thus be discussed. The results are in similar magnitude for total antibiotic use (-12%) and wait and see (14%), but the results for these secondary outcomes should be interpreted cautiously since there is a risk of type I error as we set the same significance level, 0.05, for both the primary and secondary outcomes for ease of interpretation and comparison with other studies.

In conclusion the intervention had a modest effect. The primary outcome, proportion of quinolones, decreased significantly but it cannot be attributed to the intervention. It was possible to decrease the proportion of infections treated with an antibiotic and to increase the proportion of infections handled by physicians' "wait and see" through a multifaceted educational intervention targeting both nurses and physicians. One of the questions raised, which is essential for future educational interventions, is whether it is the nurse or the physician who has most influence on antibiotic use in the nursing home setting.

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Trial registration number: NCT01054677 at http://www.clinicaltrials.gov/

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Transparency declarations

Conflicts of interest: EP is employed by Apoteket AB, The National Corporation of Swedish Pharmacies. All other authors: none to declare. Contributors: EP corresponding author. Involved in all parts of the study. Conception, design, collection, analysis and interpretation of data. Drafting the article and final approval of the version to be published. ÅV, SM and CSL involved in conception, design, analysis and interpretation of data. Revising the paper critically for important intellectual content and final approval of the version to be published. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. Data sharing: additional data are available from the corresponding author.

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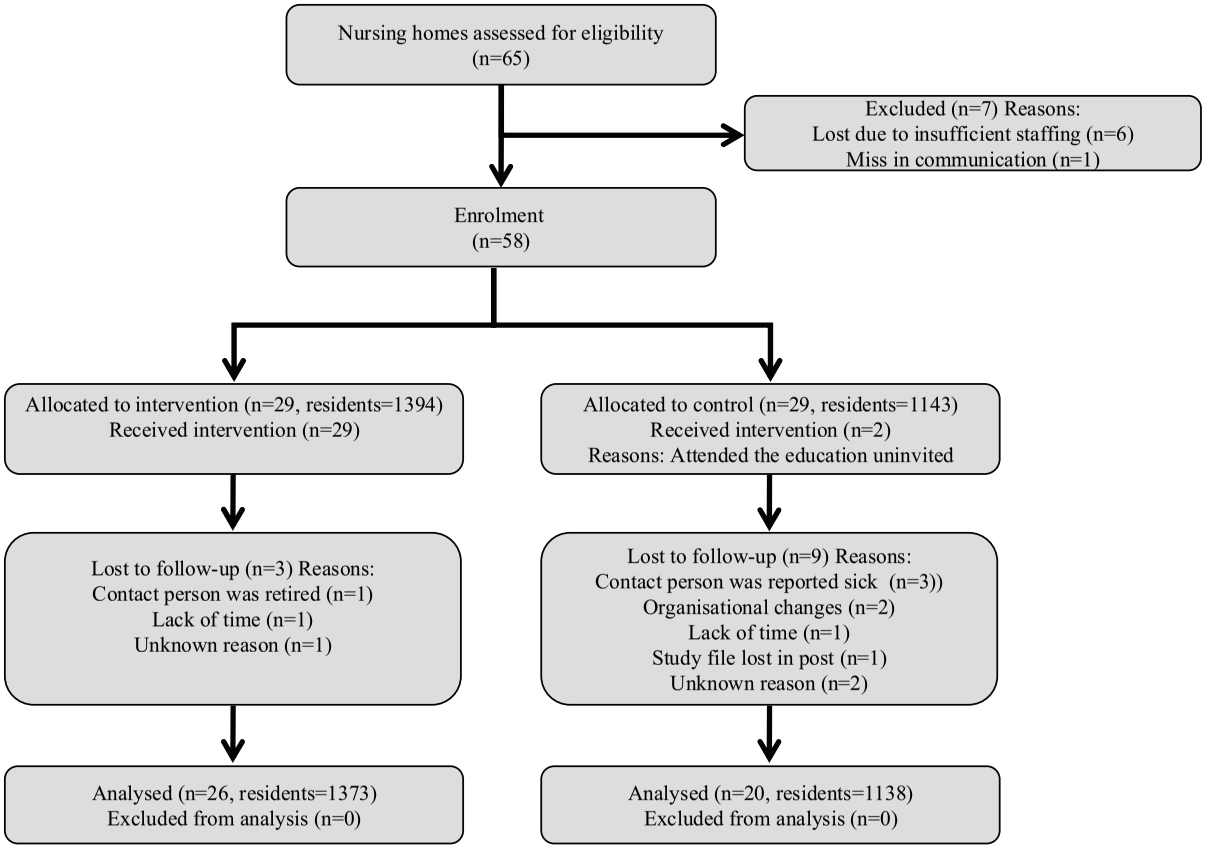

Figure 1. Flowchart of the trial.

Table 2. Results for the main outcome variables. The 95% CI were adjusted for Intra Cluster Correlation Coefficient, ICC.

Outcome, total number of observations	*Intervention*		*Difference in Intervention group* proportion (95% CI)*	*Control proportion f/n*		*Difference in Control group† proportion (95% CI)*	*The effect of the intervention‡ (95% CI)*
	2003	*2005*		*2003*	*2005*		
All residents (intervention- and control group) 2003: n=2537, 2005: n=2511	**1394**	**1373**		**1143**	**1138**		
	proportion f/n	***proportion f/n***		***proportion f/n***	***proportion f/n***		
Urinary tract infections per resident	0.141 197/1394	0.110 151/1373	-0.031 (-0.056 to -0.007)	0.152 174/1143	0.083 94/1138	-0.070 (-0.096 to -0.043)	0.038 (-0.013 to 0.089)
All infections, n=1242	**368**	**330**		**334**	**210**		
Antibiotics	0.895 325/363	0.819 258/315	-0.076 (-0.129 to -0.024)	0.884 289/327	0.931 190/204	0.048 (-0.004 to 0.100)	-0.124 (-0.228 to -0.019)
Physicians' wait and see	0.085 30/355	0.177 53/299	0.093 (0.042 to 0.144)	0.090 28/311	0.039 8/203	-0.051 (-0.096 to -0.005)	0.143 (0.047 to 0.240)
Lower UTI in women, n=434	**136**	**113**		**119**	**66**		
Quinolones	0.293 36/123	0.097 9/93	-0.196 (-0.338 to -0.054)	0.284 31/109	0.061 4/66	-0.224 (-0.394 to -0.054)	0.028 (-0.193 to 0.249)
Nitrofurantoin	0.089 11/123	0.075 7/93	-0.014 (-0.089 to 0.060)	0.073 8/109	0.136 9/66	0.063 (-0.028 to 0.155)	-0.077 (-0.242 to 0.088)

* Difference in intervention group is $d^I = p^I_{2005} - p^I_{2003}$ (p=proportion)

† Difference in control group is $d^C = p^C_{2005} - p^C_{2003}$

‡ The effect of the intervention is $e = d^I - d^C$